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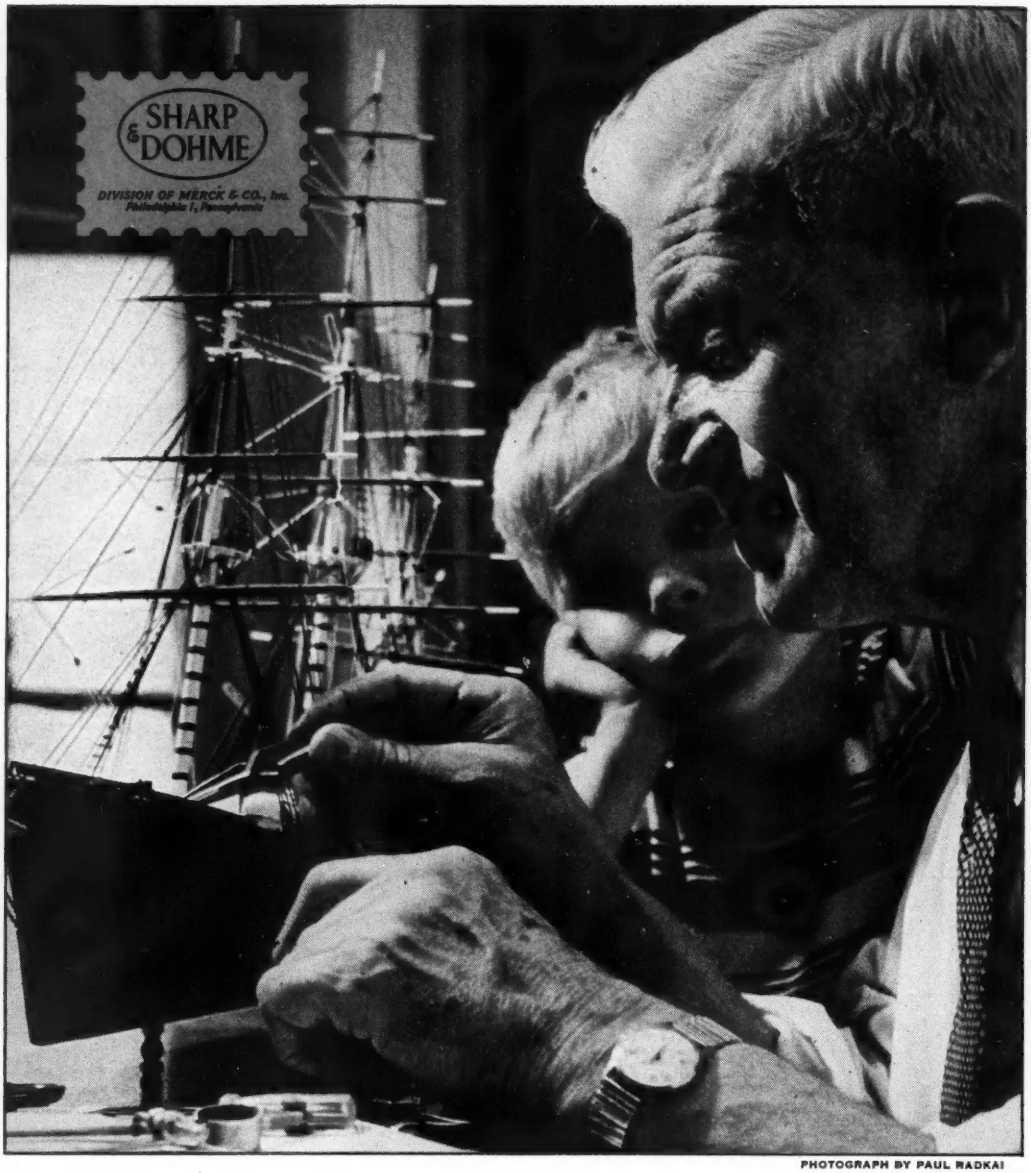

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Practical Applications of Paper Electrophoresis

THEODORE H. SPAET, M.D., San Francisco

• Paper electrophoresis of proteins is a simple, economical method well adapted to routine laboratory use. It can give important diagnostic information concerning serum proteins, and is invaluable in the differential diagnosis of diseases in which there are abnormal hemoglobins.

ANIMAL PROTEINS may be separated and characterized by a variety of methods ranging in complexity from simple salting-out procedures to the elaborate differential sedimentation obtained from ultracentrifugation. One method of protein separation, electrophoresis, is based upon the different ionic charges carried by various proteins at a given pH. If a solution of mixed proteins is placed in an electrical field, different groups of these proteins will show characteristic migration patterns, and may thus be separated and identified.

The clinical value of serum protein electrophoresis has been long known, and has been reviewed in detail by Luetscher,[11] Gutman,[6] and Fisher.[4] However, broad application of this technique has been hampered by the expense and complexity of the equipment necessary for its performance. In 1950 Durrum[1] described an apparatus by which electrophoretic separation of proteins could be accomplished on filter paper. This apparatus, simple and inexpensive in design, can be purchased from commercial sources, or can be readily constructed from available laboratory equipment. Two different types of apparatus are now in use: the original Durrum design in which the paper strips are suspended in air over a glass rod (Figure 1); and the modification suggested by Kunkel and Tiselius[9] in which sheets of filter paper are held between silicone-coated glass plates. Both methods are well adapted to routine use by a clinical laboratory.

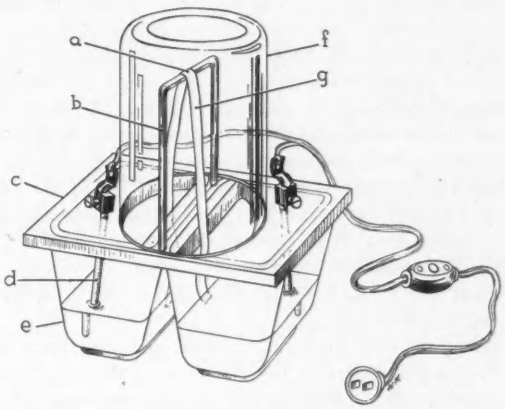

Figure 1.—Paper electrophoresis apparatus. (a) Point of application of test solution; (b) glass rod; (c) plastic cover; (d) carbon electrode; (e) glass basin containing buffer; (f) glass cover; (g) filter paper strip. (Reprinted from Spaet,[14] through the courtesy of the *Journal of Laboratory and Clinical Medicine*.)

METHODS AND MATERIALS

Both the Durrum and Kunkel-Tiselius types of paper electrophoretic apparatus were used in the present study. Detailed descriptions of these techniques have been published elsewhere.[1, 9]

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Part of the panel discussion on What's New in Pediatrics presented before the Section on Pediatrics at the 82nd Annual Session of the California Medical Association, Los Angeles, May 24-28, 1952.

In all studies, the apparatus used was charged with veronal buffer, pH 8.6. For the Durrum apparatus the electricity was 110-volt direct current taken directly from the hospital line. At this potential, adequate separation of serum proteins was obtained in 12 to 16 hours; separation of hemoglobins took 24 hours. Higher voltage can be used with the Kunkel-Tiselius apparatus, as evaporation is no problem. Radio "B" batteries connected in series, or a home-made high voltage transformer supplies 810 to 1,200 volts of potential, and runs can be accomplished in two to five hours.

For serum protein studies, undiluted serum was used without modification. Hemoglobin was rendered stroma-free and dissolved in buffer according to methods previously described.[14] Three lambda (three divisions on a pipette for counting erythrocytes) of test fluid were used. After separation, all strips were stained with bromphenol blue according to the method of Kunkel and Tiselius,[9] except that, instead of drying, they were "fixed" prior to staining by immersion in a solution of 10 per cent $HgCl_2$ in 95 per cent ethanol for five minutes.

RESULTS

Serum Proteins: As can be seen in Figure 2, at least five serum protein components can be resolved by paper electrophoresis. Fortunately, bromphenol blue combines stoichiometrically with the serum proteins so that the density of staining is proportional to the concentration of protein component. Thus it is possible to detect both the presence of abnormal proteins and deviations from the normal concentration of physiological proteins. In Figure 2 a normal pattern is shown together with patterns in three specimens of blood from patients with multiple myeloma. Each patient has an abnormal band: one at the β_2 position; one at the γ position; and one which migrates even more toward the cathode than any normal γ globulin. Such patterns may be virtually diagnostic of multiple myeloma when other studies are inconclusive.

Figure 3 shows serial patterns obtained from a 15-year-old boy with the nephrotic syndrome. This disorder resolved following cortisone therapy. The initial pattern shows protein changes which are almost peculiar to this disease, namely: diminished albumin and γ globulin combined with increased α_2 and β globulins. The succeeding patterns reflect the clinical improvement, with restoration of the protein fractions to an almost normal picture. A protein spot seen at the origin represents uncoagulated fibrinogen. This protein persisted even after apparently complete clotting in this patient, who had severe hemophilia.

Numerous other electrophoretic abnormalities of

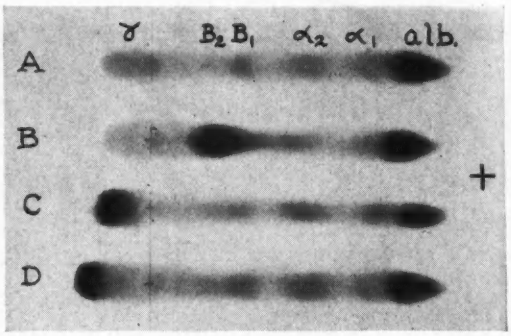

Figure 2.—Electrophoretic patterns of patients with multiple myeloma. (*A*) Normal control; (*B*) abnormal protein migrating as a β_2 globulin; (*C*) abnormal γ component; (*D*) abnormal protein which moves farther toward the cathode than any normal component.

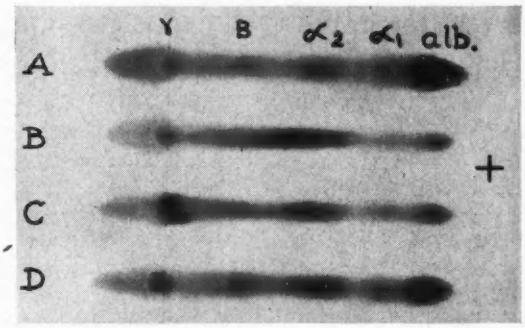

Figure 3.—Sera from a patient with the nephrotic syndrome. (*A*) Normal control; (*B*) patient prior to therapy; (*C*) one month following cortisone; (*D*) two months following cortisone. Note that initially there is a severe hypoalbuminemia together with increased α_2 and β globulins. A partial restoration toward a normal pattern is seen following therapy. (These sera were provided through the courtesy of Dr. Quentin Deming.)

the serum are found in disease, and these are readily demonstrated by the present technique. (There is not space here for an atlas of these patterns. A more detailed discussion of this subject is to be found in Luetscher's review,[11] and in Gutman's monograph.[6])

Hemoglobin: Electrophoretic studies of hemoglobin became of clinical importance in 1949 when Pauling[13] discovered different migration properties between normal hemoglobin and that of patients with sickle cell anemia. Since that time three additional electrophoretically abnormal hemoglobins have been discovered, each associated with a different morphologic pattern of erythrocytes and a different set of clinical manifestations. Each abnormality of hemoglobin appears to be transmitted according to Mendelian laws. If any pigment is "heterozygous," so that it is combined with normal hemoglobin, the patient has the respective "trait" and is free of clinical findings. Any combination of abnormal pig-

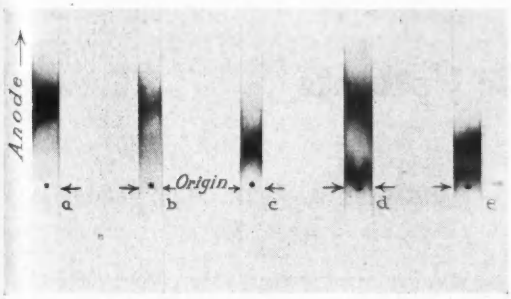

Figure 4.—Electrophoretic patterns of normal and abnormal hemoglobins. (a) Normal; (b) sickle cell trait; (c) sickle cell anemia; (d) type "c" trait; (e) combined sickle and "c" pigments. (Reprinted from Spaet[12] through the courtesy of the *Journal of Laboratory and Clinical Medicine.*)

ments, either "homozygous" or "heterozygous," appears to be associated with a hemolytic process. Sickle cell anemia is a homozygous combination of the sickle type pigment; sickle cell trait represents a heterozygous combination of normal and sickle pigments. Itano recently published an excellent review of this subject.[7]

Figure 4 shows the paper electrophoretic patterns obtained from patients with various combinations of abnormal hemoglobins. "Homozygous" and "heterozygous" combinations are clearly demonstrated. To the author the method has proved most valuable in differentiating between sickle cell anemia, and sickle cell trait with intercurrent anemia. It has also made possible the detection of cases with some of the more recently described pigments—cases that had formerly presented diagnostic problems. In one such case the patient proved to have the first reported "homozygous" type "c" hemoglobin.[16]

DISCUSSION

Electrophoresis on filter paper as described is a procedure well adapted to routine laboratory use. The cost is negligible, the technique can be learned by unskilled personnel in a short time, and many determinations may be run simultaneously. The information gained from electrophoretic studies of the serum proteins exceeds that obtained from the usual protein analyses, and the method is less laborious. It is especially adapted to pediatric needs. Since only minute amounts of blood are needed, capillary blood can be used. In the study of hemoglobin, the information provided by electrophoretic analysis cannot be duplicated by other methods.

A modification of the present technique can provide quantitation of the electrophoretically separated protein fractions. Three methods are available; the bromphenol blue may be eluted from serial segments of the paper with sodium hydroxide and measured in a spectrophotometer, according to the procedure of Kunkel and Tiselius;[9] or similar segments may be subjected to analysis by a microkjeldahl method;[10] and most recently a photoelectric scanning device has been constructed by which the density of bromphenol blue deposited in the paper is read directly.[5] Any of these methods gives reproducible results, which, however, are not strictly comparable to those obtained by older techniques.

In addition to its value as a clinical tool, paper electrophoresis has numerous research applications. Special stains have been used to measure lipoproteins, and valuable information has been obtained concerning patterns in diseases involving abnormal lipid metabolism.[3, 8] Specific serum components such as antibodies have been separated and characterized.[12, 15] A special modification of the method has provided a technique by which serum protein components may be fractionated electrophoretically in quantity.[2] These are a few of the applications which demonstrate the extreme versatility of paper electrophoresis.

REFERENCES

1. Durrum, E. L.: A microelectrophoretic and microiontophoretic technique, J. Am. Chem. Soc., 72:2943, July 1950.

2. Durrum, E. L.: Continuous electrophoresis and iontophoresis on filter paper, J. Am. Chem. Soc., 73:4875, Oct. 1951.

3. Durrum, E. L., Paul, M. H., and Smith, E. R. B.: Lipid detection in paper electrophoresis, Science, 116:428, October 17, 1952.

4. Fisher, B.: Recent contributions of electrophoresis to clinical pathology—a review, Am. J. Clin. Path., 23:246, 1953.

5. Griffiths, L. L.: A direct scanning apparatus for reading electrophoretic paper strips, J. Clin. Path., 5:294, Aug. 1952.

6. Gutman, A. B.: The plasma proteins in disease, *in:* Advances in Protein Chemistry, Ed.: Anson, M. L., and Edsall, J. T., Academic Press, Inc., New York, 1948, pp. 155-250.

7. Itano, H. A.: Human hemoglobin, Science, 117:89, Jan. 30, 1953.

8. Kunkel, H. G., and Slater, R. J.: Lipoprotein patterns of serum obtained by zone electrophoresis, J. Clin. Inves., 31:677, July 1952.

9. Kunkel, H. G., and Tiselius, A.: Electrophoresis of proteins on filter paper, J. Gen. Physiol., 89, Sept. 1951.

10. Levin, B., and Oberholzer, V. G.: Paper electrophoresis of serum proteins, Am. J. Clin. Path., 23:205, 1953.

11. Luetscher, J. A.: Biological and medical applications of electrophoresis, Physiol. Rev., 27:621, Oct. 1947.

12. Payne, R.: Personal communication.

13. Pauling, L., Itano, H. A., Singer, S. J., and Wells, I. C.: Sickle cell anemia, a molecular disease, Science, 110:543, Nov. 25, 1949.

14. Spaet, T. H.: Identification of abnormal hemoglobins by means of paper electrophoresis, J. Lab. Clin. Med., 41: 161, Jan. 1953.

15. Spaet, T. H.: Unpublished observations.

16. Spaet, T. H., Alway, R. H., and Ward, G.: Homozygous type "c" hemoglobin, Pediatrics, in press.

The Management of Allergic Patients

Practical Considerations

RICHARD A. KERN, M.D., Philadelphia

• It is important that physicians know which of their patients have allergic sensitivity, for one patient in seven will at some time have a major allergic disease. New and more serious allergic diseases are appearing, in some cases owing to sensitivity to materials used in treatment. Allergic reaction may give rise to a host of symptoms and in many parts of the body. Sensitivity to one allergen may diminish and reaction to another develop in the same patient; allergic disease may affect one organ at one time, another organ at another time.

The best way to know what patients have allergic sensitivity is to ask them. When patients are questioned, particular attention should be given to eliciting indications of personal or familial hypersensitivity.

Knowing of a patient's allergic background, a physician may be able more readily to diagnose and treat a condition that might otherwise be dismaying. Also he may be alerted as to what not to use—what bandages, sutures, drugs — in treating the patient for any condition.

WHEN A SO-CALLED SPECIALIST addresses an audience of general practitioners, he usually does three things: He tries to convince them of the importance of his specialty, which is excusable. He tries to make specialists of his audience, which is unnecessary. He forgets the broader interests of his audience, which is regrettable, because he misses a golden opportunity to give his hearers something practical to carry home. I need not stress the importance of my field in a state society that is enlightened enough to have a section on allergy. There is no point to making specialists of this group: Why invoke more competition? As for the third count, the writer is an internist with an interest in allergy, who before that was for a number of years a general practitioner, and he hopes he never loses his general viewpoint.

Please note that the title of this article refers to *allergic patients:* It is not meant to be a discussion of allergic diseases.

Do you know who in your practice are your allergic patients? It is important that you should, and for several reasons.

1. *They are numerous:* 15 per cent of them, or 1 in 7, will experience at some time in their lives a major allergic condition, such as asthma, hay fever, eczema or hives. Another 25 per cent will have a less severe, probably more obscure allergic reaction. That covers a big slice of your practice.

2. *They are peculiar people with an inherited defect:* They did not inherit an allergic disease, such as asthma, or sensitivity to an antigen such as ragweed pollen; what they did inherit was the capacity to be sensitized to things more easily than are other persons. They are born that way, they remain so until they die: The defect doesn't change.

3. *But the sensitivity pattern changes:* Old sensitivities to some things may be lost, new sensitivities can develop. Different parts of the body may become new shock organs, while parts once sensitive may lose their reactivity.

4. *The number and potency of allergens is on the increase:* This is unfortunately too true in case of many of our new and most useful remedies.

5. *New and more serious allergic diseases are appearing:* Although the usual allergic reactions are characterized by the completely reversible lesions of edema and smooth muscle spasm, more sinister necrotic irreversible lesions in blood vessel walls, as in periarteritis nodosa, are following the use of foreign sera and various drugs, with increasing frequency and fatal results. The fatal anaphylaxis from horse serum-antitoxin of the past is beginning to be replaced by equally disastrous reactions to penicillin.

Therefore, in a considerable minority of your patients, symptoms of the greatest variety and due to a legion of allergens can exist alone or in combination with almost any of the ills of the flesh, which they may modify, aggravate or minimize in endless variety.

How will you recognize your allergic patient? Ask him! If he comes to you because of pruritus ani, a condition due to multiple causes, he won't tell you

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he has hay fever, because he sees no connection. Yet if you elicit the story of hay fever, the betting odds for sensitivity to a food as a cause of the pruritus are greatly increased. You always ask your patients if they cough, belch or vomit; why not whether they sneeze, wheeze or itch? You will strike oil more often if you do.

Therefore ask every patient about a personal history of asthma, hay fever, perennial allergic rhinitis, eczema, hives, food and drug sensitivities and headaches. Naturally, you don't ask, "Have you perennial allergic rhinitis?" but rather, "When you sneeze, do you sneeze once or twice, or half-a-dozen times in a row?" A normal person is entitled to two or three consecutive sneezes, but six, routinely, are as sure to be allergic as a frank attack of asthma.

Make the same inquiry about the family, but remember that a man knows little about the family history beyond the fact that his uncle was hung for being a horse thief. It takes the women to remember that a great-aunt got hives from Jerusalem artichoke.

If the family history is positive, the patient could be allergic; if the personal history is positive, he is allergic. Then the inquiry should be extended into full details as to *relations of symptoms* to such things as time of year, day of week, time of day, weather, place, work, avocation, holidays, specific activity, tension, fatigue, particular foods, drinks, drugs, menses, intercurrent illness. Find out what the patient is exposed to in bedding, upholstery, floor coverings, animals living or dead, insecticides, cosmetics, hair dyes, residences (including dates of occupancy, heating devices and mildew in cellars). It must be pointed out that it is in history taking that the allergist shines, because he knows what to ask about and takes the time to do it.

You may now decide either that the patient's present complaint has an allergic slant, or that there is no relation at all. But in any event, be sure to *make a red check-mark before his name* as a reminder for future reference that he is allergic.

Routine physical examination may give the hint of allergic disease by the pale boggy nasal mucosa or the wheezing rales of a patient thought to have only cardiac disease.

Eosinophilia suggests allergy (its absence doesn't rule it out) and is ample reason for routine differential as well as total leukocyte counts.

The results of treatment have diagnostic value. The relief of wheezing rales by epinephrine suggests their allergic nature. The patient whose asthma stops when he is hospitalized, only to recur when he goes home, is sensitive to some inhalant in the home, usually house dust.

Of course, you should know what disease pictures could be allergic. There is time only to mention a few that are often overlooked. A fuller discussion is available elsewhere.[1]

In the ***respiratory tract***, *perennial allergic rhinitis* is commonly missed or badly treated.[2] Most people enjoy their sneezes; our grandparents took snuff to make them sneeze. When such patients do consult a physician because of increasing nasal obstruction, he prescribes nose drops or a shrinking spray, and neglects the allergic aspect. Even when polyps develop, they are repeatedly removed without subsequent search for the allergens causing recurrence. Such rhinitis, easily controlled in its beginnings, all too often leads to more serious and difficult asthma. Evanescent *hoarseness* and paroxysmal unproductive *cough* are similar expressions of chronic allergic disease. *Asthma in young children* is usually attended by fever, leukocytosis and inflamed (not pallid) bronchial mucosa, and severe attacks are called bronchopneumonia before their true nature is recognized.

The ***digestive tract*** offers many instances of allergic symptoms that are quite like those due to other causes. A few of them are cited: Recurrent crops of *aphthous ulcers* in the mouth; a wide range of *gastric episodes*, mild and severe, acute and chronic; a respectable minority of cases of *peptic ulcer* (Kern and Stewart[3]); many cases of diarrhea or constipation that are put in the diagnostic groups of *mucous* and *ulcerative colitis;* at least 20 per cent of cases of *pruritus ani. Cyclic vomiting* in children is often allergic.

In the ***skin***, all kinds of *rashes* can be of allergic origin involving things swallowed or contacted, including the very ointments used to treat them.

Allergic blood dyscrasias may be manifested as *malignant neutropenia* and many cases of *purpura*, both with and without low content of platelets, are of similar origin.

In the ***urinary tract***, such purpuric capillary bleedings can produce *hematuria* and *renal colic*, and these may be *unilateral*, suggesting organic disease. *Pain in the bladder* and *nocturnal enuresis* can arise when the bladder is the shock organ. The kidneys may be the site of *necrotizing vascular lesions* in some cases of allergic purpura, and in drug and serum sensitivity.

In the ***nervous system***, there is nothing about an allergic headache that is different from many other kinds of headache, although a fair proportion of them are in the *migraine* syndrome. The syndrome of *Menière* also includes a fair proportion of allergic nature. A rare instance of *epilepsy* (0.5 per cent of grand mal and a few more of petit mal) can be traced to an allergic cause (a pity there are so few, for in no other types of epilepsy can such complete relief be given).

In the ***cardiovascular system*** the heart is probably not the shock organ, except when coronary arteries share in *periarteritis nodosa*. But *paroxysmal auricular tachycardia* has an allergic component in a quarter of the cases, as does a rare instance of *paroxysmal auricular fibrillation*. That tobacco plays a part in *thromboangiitis obliterans* is undoubted, but that this is on an allergic basis is not proved. The author has expressed himself at length elsewhere[4] on the cardiovascular aspects of allergic states.

The **eye** supplies its quota of allergic manifestations, including many cases of *conjunctivitis, iritis, episcleritis,* and recurrent *corneal ulcer*. Allergic migraine may be associated with impairment of vision, usually evanescent, but sometimes lasting as long as 20 days and therefore suggesting a brain tumor.

The middle **ear** may suffer as a result of *eustachian block* by allergic edema.

How do you proceed with your allergic patient when you suspect an active allergic disease? If his complaint is simple, and the diagnostic possibilities few, as in many cases of hay fever, you make the necessary skin tests and establish a basis for treatment. But if the picture is more complex, and especially if your diagnostic attempts have been foiled, then waste no further time but seek an *allergic survey* by one capable to make it. This doesn't just mean a set of skin tests by some laboratory technician; you wouldn't take a technician's interpretation of an electrocardiogram. The function of the allergist is to determine causes not merely by skin tests, but chiefly by history and observation, in the light of his experience with and knowledge of allergic diseases. In the past, too many physicians thought of skin tests as the "open sesame" in allergic diagnosis, and when they failed to get a complete answer, abandoned them. Skin tests have strict limitations and many blind spots that must be reckoned with; if the reader is interested, he will find them briefly stated in a recent article by the author.[1] Nevertheless, with all their faults, they provide a valuable diagnostic tool in the hands of those experienced in their use and in the interpretation of their results.

It is hardly necessary to remind general practitioners that the *diagnosis must be complete;* the specialist is oftener in need of the warning to consider the whole patient.

The author[4] takes every opportunity to inveigh against a *common current mistake in the diagnosis of asthma*. It is assumed by some that most cases of asthma can be grouped as "extrinsic," that is, due to sensitivity to external causes; or as "intrinsic," nonallergic, due to causes within the patient, notably infection. It is indeed true that in older asthmatic persons, infection is increasingly in the picture, aided and abetted by poorer circulation, lowered resistance and perhaps beginning bronchiectasis. Chronic cough, purulent sputum, at times leukocytosis and mild degrees of fever are much in evidence. A further cause for error is supplied by the lessening reactivity of the skin as people grow older, until negative reactions are obtained to substances which still cause symptoms in the bronchial tree. All of this leads to the serious error of assuming that asthma in the aged is rarely due to allergy, but is usually "intrinsic" and infectious. Indeed Rackemann[6] has claimed that extrinsic asthma rarely begins after the age of 45.

This is grossly in error. An allergic factor, if properly sought for, can be found in the majority of elderly asthmatic persons. Even in those whose asthma begins at 70, the clue to the allergic factor is often supplied by a history of other allergic reactions, especially allergic rhinitis, that go back to early youth. That infection plays a frequent and important role in the asthma of the elderly is not denied, but that it is solely responsible is seriously challenged.

The *role of psychic factors* in conditions commonly considered allergic has been extensively and at times heatedly discussed. The author has time only to give his conclusions: Psychic factors can pull the trigger, but they do not load the gun. He has yet to see an asthmatic in whom no allergic and only psychic factors were present, and, except in rare instances, the allergic factor is preponderant.

Here are some practical points in the management of your allergic patient. The first principle of all allergic practice is that *100 per cent avoidance* of all causative allergens gives *complete clinical relief*. But putting a plastic cover on the pillow or mattress does not effect complete avoidance of the contents. Yet this mistake is being made today, times without number. It is of course absurd to change the pillow on only one of twin beds in the room, or even only on one-half of a double bed. Nor is complete avoidance achieved by the most meticulous attention to the furnishings of the bedroom, if a hot-air heating plant brings in dust from all the rest of the house. Filters in hot-air systems are not wholly efficient. Nor is avoidance of a food achieved if the ingredients of mixtures eaten away from home or in many packaged foods are unknown. Food-sensitive patients must always obey the rule: If you don't know what's in it, don't eat it.

Partial avoidance is of course better than none. Many things that are not wholly avoidable may nonetheless be much reduced in the environment; and this may be enough to achieve comfort, or to make a desensitization program effective.

For, *if symptoms persist in spite of partial avoidance, desensitization must be tried*. This involves

relatively few things: pollens, molds, a few epidermal substances, some occupational dusts and house dust. With these programs most of you are familiar. A few cautions apply: (1) *Make haste slowly;* small doses, gradually increased, spaced 5 to 7 days apart, work best. (2) *Sterilize your syringe and needle by boiling or autoclave:* alcohol can precipitate your antigen and so make it wholly or partly useless, and it doesn't protect against hepatitis. (3) For testing and treatment use an extract of dust from the patient's *own* home, not a stock house dust extract.

Complicating infection calls for surgical drainage where needed (chronic sinusitis), the use of vaccines, in selected instances of chemotherapeutic agents and of climatotherapy. Here, again, some cautions apply: *Use small initial doses of vaccine,* lest an existing bacterial sensitivity lead to severe, even serious reactions. It would be carrying coals to Newcastle to discuss climate here. But one is reminded of Robin Burns's quip that climate brings people to California and weather sends some of them away. Coastal fogs and local smog are unfavorable to most asthmatic persons, especially the elderly.

The matter of the *use of drugs* brings us back to the main point, which is the *allergic patient,* not an allergic disease. No matter why he comes to you, you must think of the *allergic* part of him before launching on any treatment, and some diagnostic procedures. No matter how you treat a sprained ankle, you must reckon with the possibility of skin sensitivity to the adhesive tape, or the more serious sensitivity to the local anesthetic you plan to inject. A surgeon who uses silk sutures in the neck of a silk-sensitive patient with goiter will be picking out silk knots for the next six months. You could cause a serious or fatal reaction to the contrast medium in your search for a lung cancer or a kidney lesion. Therefore you must heed the *red check mark before the patient's name* and follow these rules:

Don't give him drugs that can do harm because of his allergic state. Thus, don't give an asthmatic person, especially if he has fever, any drugs that will cut down an already scant and viscid sputum. That means no *atropine* and no *antihistaminics;* they can precipitate a serious, even fatal, status asthmaticus. Don't give such a patient an *opiate,* lest he die in a matter of minutes of asphyxia. Opiates, unwisely given, are still the commonest cause of death in asthma.

Don't give him a drug to which he is sensitive. Always ask him about allergy, especially about previous treatment with, or reactions to, the drug you have in mind. If he has previously received it, give it cautiously; he might be sensitive. If he has had any previous reaction to the drug, don't give it.

Don't sensitize him unnecessarily. The newer drugs, especially the chemotherapeutic agents, are all potent allergens. Each one, as it appeared, was hailed as low in toxicity and of negligible allergenic significance, only to prove quite the reverse when lapse of time had permitted its second and later courses in patients. Penicillin is no exception: It is now the cause of frequent prolonged reactions of the serum-sickness type, some of which are going on to fatal periarteritis nodosa; most recently, the severe anaphylactic reactions are being encountered, and a score or more of sudden deaths have been reported. Therefore give your allergic patient such drugs only when he really seriously needs them. Don't treat minor ailments with these potent drugs, lest a later grave illness find him deprived of their life-saving help. Don't shoot sparrows with 16-inch guns.

If your allergic patient develops an allergic reaction to a drug, stop giving the drug at once. A tragic error is to fail to realize that many drug reactions are characterized by fever, which is in turn mistaken for a continuation or aggravation of the disease under treatment, calling for further use of the drug, with disastrous results. If the drug reaction persists unduly after the administration is stopped, and especially if there develops a rising eosinophilia, there is the threat of periarteritis nodosa. This calls for the immediate use of cortisone.

This brings the discussion to its final topic: ***the use of corticotropin (ACTH) and cortisone in allergic patients.*** The following facts have been established as to the effects of these substances:

They are palliative, not curative, in allergic states. Although symptoms are held in abeyance, and even skin reactivity to allergens may be lessened and occasionally set aside, there is no diminution or change in the underlying sensitivity, and all manifestations recur upon sufficient reexposure to the cause.

They mask infection without affecting the infective agent. As Salter put it, they prove it takes two to make a quarrel: The body stops reacting with fever and symptoms, but the infection continues and can kill the non-belligerent patient.

Prolonged administration of corticotropin is followed by hypoplasia of the pituitary gland and hypertrophy of the adrenal glands; when treatment is stopped, the pituitary regains some, but not all of its loss after months, while the adrenal glands shrink to less than their former size. *Prolonged administration of cortisone* results in some pituitary hypoplasia and sharp reduction in size of the adrenal glands, and neither the enlargement nor the shrinkage is completely reversed for months. Patients after two years on cortisone are said to have died quickly from acute infections, with extreme adrenal atrophy observed at necropsy. Prolonged administration of either drug leaves the patient worse off than when he started. Remember this, above all, in children.

Corticotropin is a "good" allergen and has sensitized asthmatic persons so that reactions followed reinjection. Cortisone is a relatively "poor" allergen and only few cases of sensitivity have resulted.

The usual *untoward side effects* of both drugs are more pronounced in older patients.

Unexplained convulsive seizures, some with fatal outcome, have developed in asthmatic persons given cortisone for long periods.

The safe indications for short term (7 to 10 day) use of these substances therefore include *acute severe allergic reactions due to known and avoidable causes:* severe drug reactions; contact dermatitis, especially if severe and exfoliating; serious ivy poisoning; severe serum sickness; trichinosis; severe Loeffler's syndrome. In any of these conditions they may be life-saving. In the severest, corticotropin is given by intravenous drip. In the others, cortisone is used: 300 mg. the first day, dropping by 100 mg. daily to 100 mg. a day for a week, then tapering off by reductions of 25 mg. daily.

Additional short-term uses are: to prepare an asthmatic person for an emergency operation, to prepare a patient sensitive to Lipiodol® for a needed bronchogram, and to treat a patient in status asthmaticus, but only when all other means have failed.

Long-term therapy is justified in *allergic conditions of unknown cause that threaten life,* such as periarteritis nodosa and some severe purpuras; also in chronic beryllosis that threatens life.

Hundreds of papers have been written on such therapy in *asthma*—many of them by persons who had the drugs and some patients, but not much experience with asthma. They rushed into print with glowing reports little more justified than if someone had relieved a few asthmatic seizures with epinephrine. There is no curative effect from the treatment. It could be justified only as a short-term measure in severe cases before other therapy has had a chance to take effect, and as a long-term measure in cases in which all other treatment has failed. Yet all too often these legitimate indications are offered to cover up a short-cut around proper diagnosis and curative treatment, which are thereby improperly delayed. It is as yet impossible to pass final judgment on such cases, but the ill effects are becoming increasingly evident. Let there be none on your consciences.

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REFERENCES

1. Kern, R. A.: Diagnosis in allergic states: Principles and pitfalls, Med. Clin. N. Am., 35:1593, Nov. 1951.

2. Kern, R. A.: Perennial allergic rhinitis: The most important nasal allergy, Med. Clin. N. Am., 31:1375, Nov. 1947.

3. Kern, R. A., and Stewart, S. G.: Allergy in duodenal ulcer, J. Allergy, 3:51, 1931.

4. Kern, R. A.: Allergy in the aged, Ann. Int. Med., 35: 315, Aug. 1951.

5. Kern, R. A.: Allergic states and the cardiovascular system, Med. Clin. N. Am., in press.

6. Rackemann, F. M.: Clinical Allergy: Asthma and Hay Fever, The Macmillan Company, New York, 1931.

Health Insurance Is *Good* Medicine

EACH MEMBER OF THE California Medical Association recently received six copies of a new pamphlet titled "Health Insurance Is *Good* Medicine." Designed to help the public understand health insurance better, the pamphlet defines health insurance, reviews various plans and offers guideposts for the public's protection. Each member was asked to make this pamphlet available to his patients through his office.

The pamphlet was prepared by the C.M.A.'s Medical Services Commission and Public Relations Department.

Comments will be welcomed.

Medical Services Commission

Traumatic Pancreatitis

CLARENCE J. BERNE, M.D., and ROBERT L. WALTERS, M.D., Los Angeles

• *Traumatic pancreatitis should be considered as a diagnostic possibility when trauma to the epigastrium is followed by phenomena suggestive of intra-abdominal injury. The presence or absence of hyperamylasemia should be established immediately. Even when traumatic pancreatitis is believed to exist, any suggestion of injury to other viscera should indicate laparotomy. Retroperitoneal rupture of the duodenum may simulate traumatic pancreatitis in all respects, including hyperamylasemia. X-ray studies may be of value in differentiation.*

Non-complicated traumatic pancreatitis is best treated conservatively. Gunshot and knife wounds of the pancreas should be drained.

TRAUMATIC PANCREATITIS, characteristically a disease resulting from injury incurred in collisions of vehicles, is increasing as traffic accidents increase. Since this potentially lethal condition is often overlooked as a diagnostic possibility and in light of the fact that in many instances actions at law for compensation for damages hinge upon the diagnosis, all clinicians should be well informed regarding the diagnosis and treatment of this condition.

The experience with pancreatic trauma at the Los Angeles County Hospital was summarized as a basis for this report.

Naffziger[6] in 1943 reported nine cases of traumatic pancreatitis and stressed the importance of serum amylase determination in diagnosing the condition. In 1952 Mathewson,[4] reviewing the records of 171 cases of pancreatitis at the San Francisco County Hospital in a nine-year period, noted that 17 were the result of trauma, non-penetrating trauma in 9 instances and penetrating injuries in 8. Mathewson concluded that conservative therapy is the treatment of choice when pancreatitis is the only significant intra-abdominal lesion resulting from the injury.

Trauma to the pancreas during operative procedures in the upper abdomen may result in pancreatitis postoperatively. Stern[10] reported that the pancreas was injured more often than was recognized during operative procedures. He indicated that the pancreas was particularly liable to injury during operation on the gallbladder with exploration of the common duct, and during repair of duodenal ulcer, splenectomy, pancreatic biopsy and right nephrectomy.

Although cases in which traumatic pancreatitis was due to penetrating wounds are included in the statistics from the Los Angeles County Hospital upon which this report is based, only the group in which the disease resulted from closed injury will be emphasized. In all cases the diagnosis was made either on the basis of clinical features in association with elevation of the serum amylase or by observation at operation or autopsy. Since acute pancreatitis occurring after abdominal operations may be caused by factors other than trauma, postoperative pancreatitis will not be considered except to cite an example of one type in the discussion of treatment. All cases listed under the diagnosis of acute pancreatitis at the Los Angeles County Hospital for the period from 1939 to 1951 were used as a source of material in this report. The year 1939 was selected as a starting point because that was the first year that serum amylase determinations were used in the hospital. During the 12-year period 1,328 patients were admitted for acute pancreatitis. In 42 cases (3.1 per cent) the disease resulted from trauma: non-penetrating trauma in 18 cases and penetrating injury in 24—20 by gunshot and 4 by knife wounds.

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PATHOGENESIS

Frequently noted in the history in traumatic pancreatitis is impact of the epigastric area of the patient with the steering wheel of a car in head-on collision. Pancreatic injury may also occur when an erect pedestrian is struck across the epigastrium by the front fender of a car or when a pedestrian is knocked down by an automobile and a wheel passes over the epigastrium. Cyclists involved in accidents are peculiarly liable to pancreatic injury, the blow to the abdomen being delivered by the handlebars.

Pancreatic contusion is generally believed to involve rupture of minor or major components of the duct apparatus with consequent effects due to activity of liberated enzymes.[2, 3] The area of the pancreas most likely to be damaged as a result of a blow or crushing force is that which overlies the vertebrae. Although the middle segment of the pancreas

DATA ON 18 CASES OF NON-PENETRATING TRAUMA TO PANCREAS, LOS ANGELES COUNTY HOSPITAL 1939-1951

Case No.	Cause	Laboratory and Pathologic Change	Associated Injury
1.	Automobile accident, steering wheel.	Pancreas contused as it crossed over vertebrae.	Ribs fractured bilaterally.
2.	Automobile accident, steering wheel.	Elevated serum amylase.	None
3.	Ran into wire, blow to epigastrium.	Elevated serum amylase.	None
4.	Stream from garden hose turned on abdomen.	Elevated urinary diastase.	None
5.	Kicked in abdomen.	Elevated amylase and diastase. Developed pseudocyst. Fracture of pancreas.	None
6.	Motorcycle accident, struck in abdomen by handlebar.	Pancreas edematous with hematoma in head. Fat necrosis. Pancreas biopsied and drained. Developed collection which was drained.	None
7.	Auto accident, steering wheel.	Elevated serum amylase.	Numerous fractures.
8.	Run over by auto.	Pancreas edematous with greenish fluid under capsule. Elevated amylase.	Laceration of liver.
9.	Riding bicycle and collided with automobile.	Tail of pancreas lacerated and bleeding. Laceration sutured and area drained.	Ruptured spleen, fractured ribs.
10.	Fell down stairs.	Contusion around head of pancreas with hematoma.	Laceration of spleen, retroperitoneal hematoma, contusion of jejunum.
11.	Auto accident, steering wheel.	Elevated serum amylase.	None
12.	Run over by automobile.	Contusion of area over vertebral body.	Contusion of jeunum and mesentery, multiple fractures.
13.	Motorcycle accident, handlebar struck abdomen.	Elevated serum amylase. Developed collection which was drained.	Fractured tibia and fibula.
14.	Kicked in abdomen.	Elevated serum amylase.	None
15.	Pedestrian struck by automobile.	Pancreas edematous with fat necrosis. Elevated serum and peritoneal fluid amylase.	Hematoma of left kidney, tear in second portion of duodenum.
16.	Automobile accident, steering wheel.	Pancreatitis with fat necrosis.	None
17.	Automobile accident.	Contusion of pancreas.	Skull fracture, crushed right chest.
18.	Automobile accident, steering wheel.	Tail of pancreas lacerated and bleeding.	Ruptured spleen, laceration of serosa of right colon.

is the most vulnerable, injuries of the head and the tail do occur. In the present series there were two instances of injury to the tail of the organ, with associated rupture of the spleen in both. Since rupture of the ducts is usually within the pancreas rather than open laceration, it may be overlooked at operation. In light of the fact that injury to the pancreas commonly is masked at the time of operation by retroperitoneal hematoma, it is advisable to consider such a lesion presumptive evidence of pancreatic injury.

A process quite different from that resulting when the ducts are ruptured has been observed, as in a case in the present series: The wheel of a car had passed over the upper abdomen of the patient, and at operation the entire pancreas was observed to be swollen, but there was no hemorrhage, and the pancreas was surrounded by green tinged edema fluid. It is suggested that the cause of such a diffuse process might be multiple minor acinar ruptures secondary to an acute rise in intraductal pressure due to force applied diffusely over the extrahepatic biliary system and pancreas.

In the present series there were no recognized instances of splenic vein thrombosis, and none of chronic or recurrent pancreatitis. Neither sepsis nor abscess occurred. (Sulfonamides or antibiotics were administered in most instances.) Pseudocyst developed in three of the 14 patients with non-penetrating injury to the pancreas who lived, in one who recovered from a gunshot wound and in one who had a knife wound. Pinkham[12] noted that the development of pseudocyst is a likelihood in cases in which patients with considerable injury of the main pancreatic duct or its branches are treated conservatively.

DIAGNOSIS

Acute onset of abdominal pain following a blow to the abdomen is typical of traumatic pancreatitis. The pain is usually generalized but greatest in the epigastrium, and it may radiate through or around to the back on either side. Sometimes it is so severe as to cause suspicion of rupture of a hollow viscus. Nausea and vomiting follow and are usually persistent and may be accompanied by manifestations of shock. Upper abdominal tenderness and rigidity are characteristic and usually followed by distention. Peristalsis is decreased or absent. These symptoms are not diagnostic of pancreatic injury, for injury to viscera in the same general area may cause similar symptoms. However, if only the pancreas is involved, tenderness usually is restricted to a transverse zone across the mid-epigastrium. If hyperamylasemia is noted by laboratory study, a diagno-

sis of traumatic pancreatitis can be made tentatively.[5] It is then necessary to make sure there are no other injuries that, if present, would require laparotomy.

A particularly confusing differentiation is that between traumatic pancreatitis and retroperitoneal rupture of the duodenum.[1, 8, 9] Differentiation is essential because duodenal rupture demands immediate surgical correction. The two lesions may coexist. Traumatic rupture of the duodenum like traumatic pancreatitis often follows a blow to the upper abdomen and the serum amylase may be elevated due to escape of pancreatic secretion from the duodenum into the retroperitoneal space and its subsequent absorption into the blood. An x-ray film of the abdomen may be helpful in differentiation. Retroperitoneal rupture of the duodenum may produce gas in the retroperitoneal tissues appearing either as diffuse emphysema or as gas along the right psoas muscle. In traumatic pancreatitis there may be distention of a segment of the bowel, either of the transverse colon or the upper jejunum, due to enzymatic mesenteritis. If duodenal rupture is suspected but no evidence of retroperitoneal gas can be seen in the x-ray film, Lipiodol® should be injected through an inlying nasogastric suction tube and another film taken to determine the presence or absence of extraluminal Lipiodol.[8] Barium sulfate should not be used as a contrast medium because of its objectionable features as a foreign body. When the area is visualized at laparotomy, either lesion may be associated with retroperitoneal hemorrhage that masks the visceral injury. However, the hemorrhage may be slight, and with either lesion there may be greenish edema fluid in the upper retroperitoneal tissues.

When clinical features logically suggest pancreatic trauma, it is mandatory that the presence or absence of hyperamylasemia be established. This is most satisfactorily accomplished by making several measurements of the amylase content of the blood. If renal function is unimpaired, the urinary diastase content will indicate the amount of amylase in the blood. If possible, both tests should be carried out. Such observations are of importance in even relatively mild injuries, to establish for medicolegal reasons that such injury has occurred.

TREATMENT

Traumatic pancreatitis will heal spontaneously unless there is persistent leakage of some part of the duct system. Sufficient leakage will lead to the formation of a pseudocyst ("pancreatic collection"[7]), almost always in the lesser omental bursa. The dynamic activity of the collection may be mild to severe, depending upon the amount of leakage. Surgical drainage must be carried out.

Non-operative management is preferable for uncomplicated traumatic pancreatitis. The essentials of this regimen are the same as for spontaneous pancreatitis: Nasogastric suction, maintenance of fluid and electrolyte balance by intravenous therapy and the use of anticholinergic drugs. A "wide spectrum" antibiotic should be given. Demerol® is the drug of choice for control of pain.

If it is not possible to determine that there is no associated visceral injury that would necessitate surgical treatment, laparotomy should be done. In such circumstances the problem of specific treatment to the pancreatic injury arises, as it does also when unsuspected injury of the pancreas is noted fortuitously in the course of operation for another condition. It is the authors' opinion that in either instance drainage is indicated if there is laceration of the pancreas, lest escaping fluid gather in the peritoneal sac and cause complications. If the surface of the pancreas appears to be intact, however, it is recommended that the abdomen be closed without pancreatic drainage, for in approximately 80 per cent of the cases due to non-penetrating trauma the laceration is not sufficient to be productive of pseudocyst. Moreover, without a demonstrable laceration precise drainage cannot be accomplished. If a pseudocyst develops later, drainage then can be accomplished with adequate precision.

When the abdomen has been opened and traumatic pancreatitis observed, the question arises whether or not to decompress the biliary duct system. Because often there is a common channel, it seems logical, theoretically, that cholecystostomy should decompress the pancreatic ductal apparatus in most cases.

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REFERENCES

1. Cohn, I., Hawthorne, H. R., Frobese, A. S.: Retroperitoneal rupture of the duodenum in non-penetrating abdominal trauma, Am. J. of Surg., 84:293-301, Sept. 1952.

2. Howard, J. M.: Surgical physiology of pancreatitis, S. Clinics of No. America, 29:1789-1800, Dec. 1949.

3. Ivy, A. C., Gibbs, G. E.: Pancreatitis: A review, Surgery, 31:614-642, April 1952.

4. Mathewson, C. Jr., Halter, B. L.: Traumatic pancreatitis with and without associated injuries, Am. J. Surg., 83: 409-411, March 1952.

5. McCorkle, H., Goldman, L.: The clinical significance of the serum amylase test in the diagnosis of acute pancreatitis, Surg., Gynec. and Obst., 74:439-445, Feb. 16, 1942.

6. Naffziger, H. C., McCorkle, H. J.: The recognition and management of acute trauma to the pancreas, with particular reference to the serum amylase test, Ann. Surg., 118: 594-602, Oct. 1943.

7. Pinkham, R. O.: Pancreatitic collections (pseudocysts) following pancreatitis and pancreatitic necrosis, Surg., Gynec. and Obst., 80:225-235, March 1945.

8. Siler, V. E.: Management of rupture of the duodenum due to violence, Am. J. of Surg., 78:715-727, Nov. 1949.

9. Simpson, J. A.: Traumatic retroperitoneal rupture of the duodenum, Brit. J. of Surg., 148:483-485, April 1950.

10. Stern, E. L.: Traumatic injuries to the pancreas, Am. J. of Surg., 8:58-74, Jan. 1930.

The Treatment of Infectious Diseases

Advances in the Use of Antimicrobial Drugs

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• Penicillin remains the most useful antibiotic for treatment of infections due to organisms sensitive to this drug because of its bacteriocidal properties and its freedom from toxicity. Enormous doses may broaden its antibacterial spectrum and it may act synergistically with certain other drugs.

New penicillin compounds have been developed which serve such special purposes as (1) concentration in lung tissue, (2) maintenance of therapeutic concentrations in the blood for long periods after injection, (3) avoidance of allergic reactions and (4) prolongation of therapeutic content in the blood after oral administration.

Erythromycin and carbomycin may be effective against bacterial infections not sensitive to other antibacterial drugs.

Streptomycin combined with dihydrostreptomycin is less toxic than is either drug used alone.

Isoniazid is a valuable antituberculosis drug, especially when combined with streptomycin.

Viomycin may be useful in treating tuberculous infections that have become resistant to other specific drugs.

THIS PRESENTATION is intended to evaluate briefly some recent significant advances in specific antibacterial therapy with penicillin, erythromycin, carbomycin, streptomycin, viomycin and isoniazid.

The commanding position of penicillin among antibiotics has been maintained and even advanced by recent developments. It has at least four outstanding valuable attributes: (1) It is bacteriocidal in high concentrations. (2) High concentrations in blood and tissue are attainable, since dosage may be increased almost without limit, if necessary, without toxic effect. (3) High concentrations also broaden the spectrum of activity of this drug. (4) Penicillin acts synergistically with some other drugs.

Bacteriocidal action may be necessary for the cure of some chronic infections, such as subacute bacterial endocarditis, although bacteriostasis is adequate for the cure of some acute diseases with natural immunity mechanisms, such as pneumonia. Massive doses of penicillin, from 10 million to 100 million units daily, given intravenously, may have bacteriocidal effects not possible with conventional doses. When it is given in such quantities the sodium salt of penicillin G should be used rather than the potassium salt to avoid serious potassium intoxication.

Although it has been referred to as a narrow spectrum antibiotic, penicillin may better be designated a highly specific antibiotic, for it may be much more potent than any other substance against certain infections. When given in massive doses it is effective against many kinds of pathogenic agents that are not affected by usual doses. A bacteriologist is often an indispensable consultant to a clinician dealing with serious bacterial infections, for the best choice of drug or combination of drugs and the dose necessary may depend upon sensitivity tests in vitro.

The action of penicillin is sometimes considerably enhanced by use of another antibacterial drug with it. Bacitracin or streptomycin combined with penicillin may kill bacteria which are relatively insensitive to either of these antibiotics alone. It is also true that combinations may be less effective than penicillin alone, especially when the second drug is one of the so-called broad spectrum antibiotics, such as aureomycin, chloramphenicol, or terramycin.

The clinical usefulness of penicillin has been enhanced with the appearance of new special purpose penicillin compounds. Four types of such compounds that have been developed recently deserve special mention:

1. Penethamate hydriodide (penicillin G diethylaminoethyl ester hydriodide) concentrates in lung tissue and in pulmonary secretions more than in other organs. Chronic pulmonary infections, including bronchiectasis and pulmonary abscess, may respond to treatment with this ester of penicillin in moderate doses. Large doses of procaine penicillin may yield similar results. As iodine content of penethamate hydriodide is considerable, the drug may be useful as an expectorant, but it cannot be given

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to patients who have idiosyncratic sensitivity to iodides.

2. Dibenzyl-ethylene-diamine dipenicillin (DBED dipenicillin) is most remarkable for the fact that a single injection (600,000 to 1,200,000 units) may maintain the content of the drug in the blood at a low therapeutic level for from two to four weeks. Its greatest field of usefulness is thought to be in the prophylaxis of rheumatic fever but it opens a possible field for study of specific prevention of some other infectious diseases as well.

3. Allergic sensitivity to penicillin is frequently troublesome and substantial progress toward prevention of such reactions has been made since the appearance of hypoallergic penicillin compounds, especially 1-ephenamine penicillin and penicillin "O." These compounds may be tolerated by patients with a history of cutaneous allergic reaction to penicillin.

4. Oral penicillin therapy is more feasible now that sustained content in the blood may be realized for at least eight hours after a single dose of 200,000 units of either dibenzyl-ethylene-diamine dipenicillin or a combination of penicillin G with probenecid.

Erythromycin and carbomycin are new antibiotics with a spectrum of activity similar to that of penicillin. It is by no means clear when they should be chosen in preference to the better known antibacterial drugs unless in vitro tests indicate that the organism in question is more sensitive to one of the new preparations. Many penicillin-resistant staphylococci and non-hemolytic streptococci are found to be sensitive to erythromycin and to carbomycin. There is some cross resistance between erythromycin and carbomycin but the two drugs are not identical. They do not have the same range of bacteriocidal possibilities that penicillin has, and unlike penicillin they cannot be given in massive doses.

The neurotoxic potentialities of streptomycin have now been reduced substantially by the practice of combining streptomycin with dihydrostreptomycin. The logic of this combination is very simple: Since streptomycin toxicity is ordinarily limited to an effect upon functions of the vestibular branch of the eighth cranial nerve, and the toxicity of dihydrostreptomycin, which has similar therapeutic effect, ordinarily affects only the auditory branch of this nerve, combining them in equal amounts greatly reduces the risk of toxic damage without sacrifice of therapeutic value. Animal experiments and clinical studies have shown that this advantage is realized.

Streptomycin neurotoxicity is rarely observed, regardless of the type of streptomycin used, if dosage is limited to 1 gm. given every second or third day; and this amount is adequate to control most chronic tuberculous infections when combined with para-aminosalicylic acid (12.0 gm. daily). These drugs are usually given for a period of one year or more in the treatment of chronic pulmonary tuberculosis.

Nearly all patients with active tuberculosis now receive specific antibacterial drug therapy and often conservative collapse therapy. Pulmonary resection of residual foci of inactive disease remaining after nine to twelve months of specific medical treatment is frequently recommended as a means of preventing subsequent relapse. Such treatment more nearly approaches curative and definitive therapy than any used heretofore.

Isoniazid has now been studied clinically for more than a year in many institutions and its usefulness and limitations are becoming well established. When used alone it is often inadequate to control chronic tuberculosis because of the early appearance of resistant bacilli, frequently within two or three months. When it is combined with streptomycin there is striking added therapeutic benefit and some delay in the appearance of resistant bacilli. Isoniazid is an extremely valuable preventive of tuberculous complications of pulmonary resection, and some surgeons have urged that if intrathoracic operation is contemplated, isoniazid not be used until the time of operation. Isoniazid diffuses through tissues more readily than do other antituberculosis drugs and appears in the cerebrospinal fluid freely. For this reason it has become a very valuable addition to streptomycin and para-aminosalicylic acid in the treatment of tuberculous meningitis.

Viomycin, a new antibiotic useful for the treatment of tuberculosis, is now available commercially. Its precise place in relation to other antituberculosis drugs is not clear, except that it is of value in the treatment of infections that have become resistant to the more familiar drugs. With the appearance of new specific drugs such as isoniazid and viomycin, the plight of patients with an infection resistant to streptomycin and para-aminosalicylic acid is not so serious as it formerly was. The need for precise bacteriologic studies of drug resistance has become obvious and has been met in most hospitals and sanatoriums.

490 Post Street.

Radiological Aspects of "Collagen" Diseases

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• The collagen diseases, an ill-defined group of clinical entities, have as their basis a generalized alteration of the connective tissue, especially of its extracellular components. They include periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis, scleroderma, rheumatic fever and rheumatoid arthritis.

The radiological findings in a series of cases of these diseases were reviewed.

In 28 cases of periarteritis, 20 cases showed some abnormal findings in the thorax. These included pleural effusions, pulmonary changes, pericardial effusions and cardiac enlargement.

In 32 cases of disseminated lupus erythematosus, thoracic findings were noted in 21. They resembled the changes found in periarteritis.

In some 25 cases of scleroderma, diverse radiological findings were noted. These included "cystic" changes in the lungs (one case) and pulmonary "hives." In the intestinal tract esophageal and small bowel alterations were found, both ectatic and stenotic. In the soft tissues of the "pressure areas" variable degrees of calcification were observed.

Dermatomyositis is the rarest of the collagen disease group; only one autopsy-proven case is available for study. Chest x-rays taken a year before death showed slight cardiac enlargement. The lungs were clear.

In acute rheumatic fever, x-ray examination may disclose pericardial or pleural effusion, and so-called rheumatic pneumonitis; the latter has no specific diagnostic features. Soft tissue swellings may develop around some of the joints.

In rheumatoid arthritis, joint changes are numerous and fairly characteristic, and are followed in many cases by fibrous or bony ankylosis and deformities of considerable degree.

Awareness of the commoner radiological changes in this entire group of diseases should result in earlier establishment of diagnosis, especially in the more obscure examples.

As EVOLUTION PROCEEDS, some diseases are conquered or become less common while others develop or become recognizable as separate entities. For some of the latter order a nomenclature is invented and the clarity of epithet is usually in direct proportion to the knowledge of etiologic delineation. Among diseases for which the nomenclature is as yet inept—for the reason indicated—are the so-called collagen diseases.

What are the collagen diseases? What are their radiologic aspects? What is ostensibly new concerning them? Some progress toward answers to some of these questions may be made by reviewing the cases of 86 patients with diagnosis of collagen disease who were observed in hospital practice during the last several years.

The collagen diseases are a group of disorders characterized anatomically by generalized alterations of the connective tissue, especially of its extracellular components. The following are currently accepted as members of this group: Periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis, scleroderma, rheumatic fever and rheumatoid arthritis.

The term *polyarteritis* is synonymous with *periarteritis nodosa.* Because of the predominance of vascular changes, this disorder (and, to a lesser extent, generalized lupus erythematosus) may also be referred to as *visceral angiitis.* Disseminated lupus erythematosus is also known as *acute lupus erythematosus* or *generalized lupus erythematosus.*

Becker[2] and others suggested that since the systemic manifestations of Schonlein-Henoch *purpura,* of *erythema nodosum* and of certain cases of *glomerulonephritis* show similar involvement of connective tissue, they too may belong to this group of diseases. Ehrick[4] and associates, on the basis of animal experiments, would also include *serum sickness.* Kampmeier[10] suggested that the necrotic changes found in afferent renal arteries in both malignant hypertension and periarteritis nodosa have more than coincidental relationship. Stewart[18] expressed belief that thromboangiitis obliterans and ulcerative colitis also are collagen diseases.

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ETIOLOGY AND PATHOLOGY

The cause of the collagen diseases is not known. Several investigators have produced fibrinoid changes of connective tissue experimentally by mechanical

and by chemical means.[3] These observations tend to invalidate the supposition that hypersensitivity is the sole cause of collagenous degeneration. Indeed, it has been observed that undue significance should not be attached to the occurrence of fibrinoid changes in localized connective tissue collagen. Pathologically this is merely a form of degeneration, of unspecified cause, and it occurs in a wide variety of dissimilar diseases. This fact of course greatly diminishes the clinical usefulness of the term *collagen disease.* However, until a better term is devised and until more is known about the fundamental nature of the diseases in question, it is probably justifiable to continue the use of the makeshift. In this connection, it is to be noted that the microscopic findings are not merely of changes in the collagen fibers alone but of changes in the connective tissue elements as a whole.

Histologically, connective tissue consists of cellular elements and extracellular substances. The cellular elements consist of fibrocytes and fibroblasts, macrophages, lymphoid cells, mast cells and various other leukocytes. The extracellular substances are composed of an amorphous ground substance and three known types of fibers, collagenous, reticular and elastic. The basic lesion in the collagen diseases consists of a swelling of the interfibrillary ground substance as well as swelling of the fibers themselves. The location of these basic lesions and the type of response of the adjacent tissues are somewhat different in the different collagen diseases, and constitute the anatomic basis by which they may be at least partly distinguished.

Not all clinical subdivisions of the collagen diseases are clearly demarcated. Sometimes, at necropsy, lesions peculiar to or predominant in some of the different entities may be observed in one and the same subject. For example, a fatal case may show: (a) Chronic skin lesions, as in scleroderma, (b) atrophy of skin, and degeneration of muscle, as in dermatomyositis, (c) proliferation of endothelial capillary tissue, as in disseminated lupus erythematosus, (d) non-bacterial verrucous endocarditis,* (e) infiltration and dilatation of arterioles, as in periarteritis nodosa, (f) pericardial changes, as in rheumatoid infection, and (g) articular and tenosynovial changes, as in rheumatoid arthritis.

A case embodying all these diverse manifestations was reported by Kampmeier.[10]

Miale[14] mentioned that Krupp first emphasized a characteristic urinary finding in "visceral angiitis"; he found the pattern in 14 of 21 cases of periarteritis nodosa and disseminated lupus erythematosus. It consists of the simultaneous presence of elements usually characteristic of the early stages of nephritis (erythrocytes and erythrocytic casts), and elements usually seen in the chronic stage (broad casts, waxy casts, fatty casts, and "oval fat bodies"). This finding has been referred to as "telescopic urinary sediment."

*Non-bacterial verrucous endocarditis, as in Libman-Sacks syndrome,[11] is now known to be part of the changes occurring in disseminated lupus erythematosus.

CLINICAL TYPES AND SOURCE OF MATERIAL

The types of collagen disease to be discussed herein include periarteritis nodosa, generalized lupus erythematosus, dermatomyositis, and scleroderma. Only brief mention will be made of the two more common entities, rheumatic fever and rheumatoid arthritis.

The cases studied were obtained by a review of the files in the x-ray departments and the record rooms at the San Francisco Hospital and the Stanford University Hospital.† The period covered is approximately 15 years, a majority of the cases having been indexed in the last 10 years.

Periarteritis Nodosa (Polyarteritis)

Periarteritis nodosa is frequently and more correctly called polyarteritis as there is actually a widespread *poly-* rather than *peri*arteritis, affecting chiefly the medium-sized and smaller arteries of the body. Pathologically there is a degeneration of the collagenous tissue in the walls of the vessels, sometimes with necrosis of the media, rupture of the elastic lamina and infiltration of inflammatory cells and eosinophils into all the vascular layers. When this infiltration of the arterial coats is localized, or is followed by local fibrosis, or the development of small aneurysmal dilatations, nodular changes develop (giving rise to the term *nodosa*).

Clinically the signs and symptoms are determined more by the distribution of the involved arteries than by the disease process itself. Almost any clinical condition may be mimicked. However, a polysystemic involvement with chronic fever, leukocytosis, eosinophilia and secondary anemia suggests the condition, and is an indication for skin and muscle biopsy.

Radiologically, findings may or may not be present, depending on which systems happen to be involved, and also on the acuteness and degree of involvement. Cardiac enlargement and/or pericardial effusion occurs. The respiratory system may show massive symmetrical or non-symmetrical edema in severe acute cases. In others, small hazy shadows or non-confluent patches of edema (pulmonary hives) may be scattered throughout the lung fields, usually peripherally and at the bases.[1] Some observers[5, 17] have reported cases in which the nodulation was most pronounced centrally. In addition

†The authors are indebted to Dr. H. S. Kaplan for permission to review the latter.

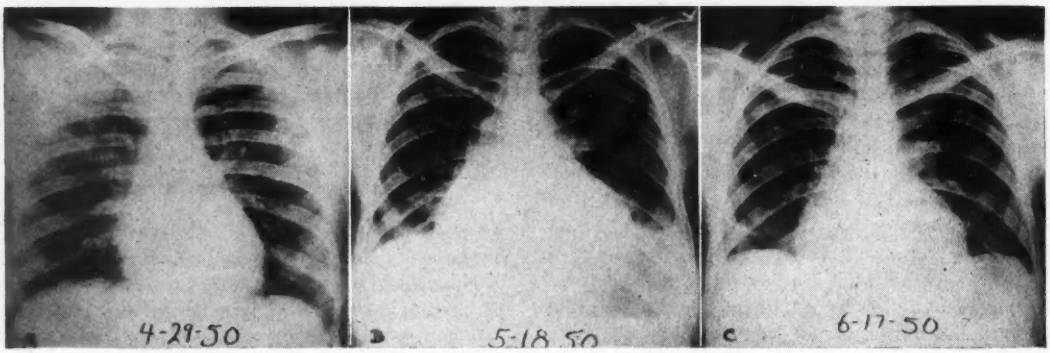


Figure 1.—Periarteritis nodosa. Acute pericardial and bilateral pleural effusions developed during a chronic illness of two years. Biopsy positive. The patient was a white woman 26 years of age with arthralgia, myalgia, fever and gangrene of tips of fingers and toes. *A.* Chest film negative; pericardial friction rub present. *B.* Pericardial and bilateral pleural effusions. *C.* Improvement; also improved clinically, under cortisone therapy.

to the nodular densities, the pulmonary linear markings may be accentuated, particularly the hilar and basal ones. Pleural effusion, secondary to pneumonitis or pulmonary infarction, is reportedly not uncommon.

X-ray examination of the abdomen is frequently requested since abdominal pain is one of the commonest early symptoms. A triad of myositis, abdominal pain and loss of weight has been referred to by some investigators. The abdominal films usually show either no abnormality or some collections of gas suggesting paralytic obstruction (so-called adynamic ileus). Very rarely, there may be a perforated ulcer, intestinal infarction or pancreatic necrosis. In one of the cases in the present study there were both intraperitoneal and retroperitoneal bleeding due to ruptured aneurysm of a small mesenteric vessel, secondary to "healed" arteritis. Hypertension was present, the blood pressure 200 mm. of mercury systolic and 140 mm. diastolic. The patient also had multiple duodenal ulcers.

Renal lesions are the commonest of all the systemic lesions, being present in 80 per cent of the cases.[13] Occasionally hypertension or hematuria may be so prominent that intravenous pyelograms are requested. These usually show either normal or decreased function.

The records of 29 cases of periarteritis nodosa were reviewed. In 28 of these, films of the chest were available and disclosed the findings shown in Table 1. It is to be noted that in some cases there was more than one abnormality observed (for example, pericardial, pleural and pulmonary lesions).

In one case, in which -ray films had shown cardiac enlargement, pulmonary congestion and pleural effusion, both polyarteritis and rheumatic heart disease (mitral and aortic stenosis with insufficiency) were noted at autopsy.

None of the x-ray findings noted in Table 1 are

TABLE 1.—*Observations in x-ray films of chest in 28 cases of periarteritis*

No evidence of disease		9
Evidence of disease		19
*Cardiac enlargement	4	
Pericardial effusion	4	
Pleural effusion	4	
Pulmonary changes	14	
Parenchymal nodules, patches, etc.	4	
Pulmonary congestion, passive	6	
Accentuated markings, ? arteritis	3	
Pulmonary edema, massive	1	

*In some of the cases in which "cardiac" enlargement was observed there may also have been some pericardial effusion.

diagnostic *per se* of periarteris nodosa, but the presence of pulmonary, pleural or cardiopericardial changes in a patient with involvement of other systems should cause one to bear the possibility of a collagen disease in mind.

In the 29 cases, adequate radiological records of systems other than the cardiorespiratory were limited. In two cases, hepatomegaly and in two cases splenomegaly were noted by physicians in the Department of Radiology. X-ray evidence of mild paralytic ileus was noted in one case, and in three there was peptic ulcer (one gastric and two duodenal). No cases of gross renal enlargement were recorded, but in one case poor function was shown by excretory urography. No bone changes were noted; in three patients there was x-ray evidence of articular disease (synovial thickening in two and rheumatoid arthritis in one). Biopsy or necropsy material compatible with the diagnosis of periarteritis nodosa was available in 17 out of the 29 cases. In seven cases biopsy reports were negative for periarteritis nodosa but the clinical evidence was outstanding and two of the patients died apparently of the disease.*

*Most of the histopathological studies referred to in connection with the cases reported in this paper were made by members of the staff of the Department of Pathology, Stanford University School of Medicine. In a few instances material was reported upon by members of the University of California staff at the San Francisco Hospital, to whom the authors are indebted.

The following are illustrative cases:

¶ A 26-year-old white woman with migratory pains in the joints, low-grade fever, myalgia and patchy gangrene of some of the fingers and toes was known to have had periarteritis nodosa for two years. Upon radiographic examination of the chest no abnormality was noted. Reexamination two and one-half weeks later showed small bilateral pleural effusions and pericardial effusion. A month later, after cortisone therapy, clinical and radiographic improvement was present. In this case there was acute development of pleural and pericardial lesions during the course of a chronic, multiple-system disease. Biopsy of skin and muscle was positive for periarteritis nodosa.

¶ The patient, a 63-year-old man, had had fainting spells of unknown cause for a few weeks, and pain and stiffness of the shoulders and knees since a fall one month before admittance to hospital. Initial x-rays of the chest showed only slight left ventricular enlargement. Two days later, films showed bilateral pleural effusion and pulmonary congestion. Clinically the patient had become acutely ill, with high fever (up to 103.1 degrees F.), but there was no evidence of cardiac failure. X-ray examination four weeks later showed clearing of the congestion and effusions, but the patient was failing generally. Abnormalities then were noted in the urine (the so-called telescopic sediment) and the possibility of "visceral angiitis" was considered. The patient recovered partially and was discharged. Biopsy of skin and muscle was reported negative.

¶ A 34-year-old white woman had had asthma for one year and numbness of the left leg and pain in the left foot for six months. She was found to have splenomegaly, eosinophilia and a renal lesion, with casts and cells. X-ray films of the chest showed pulmonary nodulation, fibrosis and emphysema. Biopsy of skin and muscle was reported negative. Pronounced clinical and radiological improvement occurred within three days after cortisone was started. The patient was discharged improved.

¶ A white longshoreman 45 years of age entered the hospital with chilliness, fever (101 degrees F.), mild cough, pain in the chest and dyspnea. He had dermatitis of two years' duration on the leg, with local ulceration. Pain in the right upper quadrant of the abdomen, pronounced enlargement of the liver and massive hematuria developed. The blood pressure was 180 mm. of mercury systolic and 80 mm. diastolic. The urea content of the blood was 27 mg. per 100 cc. The number of leukocytes was within normal limits. X-ray films showed clouding of the right upper lobe and of the left midlung field, interpreted as pulmonary edema. Moderate splenomegaly was noted on an abdominal film. Nine days after admittance the patient was clinically and radiologically improved. Biopsy was not performed. A year later, no abnormality was noted in an x-ray film of the chest.

¶ The patient was a 40-year-old white man with clinical diagnosis of rheumatoid arthritis. X-ray films showed cardiomegaly, predominantly left ventricular, and bilateral pleural effusion. The patient died shortly after examination, apparently from cardiac failure. Autopsy showed:

A. Diffuse collagen disease with
   1. Polyserositis (peritoneal, pleural and pericardial fluid)
   2. Rheumatic heart disease (aortic valve stenosis)
   3. "Wire-looping" of renal glomeruli (as in lupus erythematosus)
   4. Rheumatoid arthritis
   5. Periarteritis nodosa (of pulmonary, thyroid and testicular arteries)

B. Pulmonary emphysema (and fibrosis)

C. Generalized arteriosclerosis (coronary, aortic and renal).

In this case there was a combination of four types of "collagen" disease—periarteritis nodosa, lupus erythematosus, rheumatoid arthritis and rheumatic carditis.

Disseminated Lupus Erythematosus

Disseminated lupus erythematosus, or systemic lupus erythematosus, is a disease most commonly seen in women, and in the ages of 20 to 40. It is characterized by a cutaneous eruption, most often in the form of discoid lesions—with a butterfly distribution over the nose and cheeks—along with varying degrees of visceral manifestation, notably in kidneys, heart, spleen and lungs. The skin lesion is frequently photosensitive, being made worse by sunlight or ultraviolet light or such light-sensitizing drugs as the sulfonamides. Patients may have fatigue, arthralgia and fever. The laboratory findings include leukopenia, accelerated sedimentation rate, "telescopic" urinary sediment and the presence of so-called lupus erythematosus cells.[9] These cells, found only in this disease, are seen in various preparations of blood and bone marrow and are reportedly large leukocytes containing phagocytosed material resulting from lysis of the nuclei of other leukocytes.

Pathologically, there is predominant involvement of the smaller arteries and arterioles. Polyserositis is common, with pericardial lesions the most frequent. In the heart itself, lesions predominate in the valvular structures and the mural endocardium. The kidneys, when involved, tend to be enlarged. The glomerular vessels show the so-called "wire-loop" appearance due to eosinophilic thickening of the vascular loops within the glomeruli. Occasionally the renal changes resemble those of glomerulonephritis or periarteritis nodosa. Periarterial fibrosis may be seen microscopically in at least half of the cases. The lymph nodes are said also to be frequently involved, showing "free hematoxylin-staining bodies."[11]

Radiologically, abnormalities may be noted in the urinary and respiratory tracts. When a patient with hypertension has unusually large kidneys, the possibility of disseminated lupus erythematosus rather than a chronic glomerular nephritis must be considered. Patients with the latter condition tend to have small or contracted kidneys. Pulmonary involvement is remarkable for its frequency and its atypical course. Rakov and Taylor[16] and Foldes[6] described chronic interstitial pneumonitis which leads to atelectasis (due to interstitial edema and inflammation resulting in obliteration of some alveoli)—termed atelectasizing pneumonitis. These lesions are regarded as different from the ordinary pyogenic and fibrinous types of bronchopneumonia which so frequently complicate the terminal stages of lupus erythematosus.

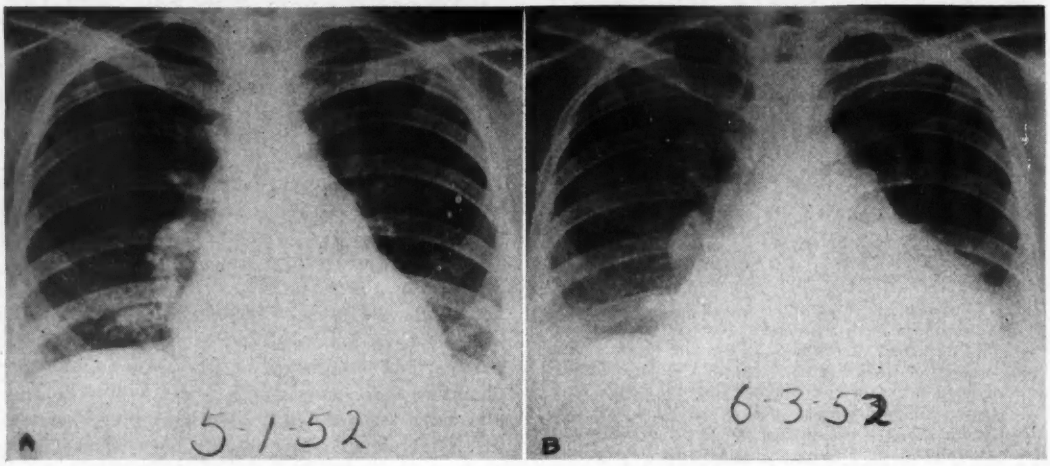


Figure 2.—Disseminated lupus erythematosus, showing right basal nodular densities, with pleural and pericardial effusions. The patient was a 25-year-old white woman. Peripheral arthritis, hematuria, fever and pericardial friction rub, three days. *A.* Small nodular densities, right base, small bilateral pleural effusions, enlarged heart-vessel shadow. *B.* Right basal nodulations obscured or not present; effusions increased. Discharged unimproved.

Thorell[20] reviewed the x-ray films in 15 cases of disseminated lupus erythematosus and found that in eight cases there were pleural or pulmonary parenchymal changes, or both. The pleural effusions were generally small; the pleural thickening more or less irregular. These pleural changes varied in extent in relatively short periods. The parenchymal changes consisted of small areas or patches of increased density, mostly subpleural, especially in early and moderately advanced cases. Thorell used different oblique projections to bring out the subpleural location of the lesions. He expressed the opinion that a combination of pleural and subpleural change ought to lead to the correct diagnosis even if the changes in themselves were not characteristic.

In the series herein reviewed, pleural and pericardial effusions were the commonest findings in lupus erythematosus. The pulmonary parenchymal changes varied from localized accentuated markings, nodules and patches, to extensive edema.

The records of 35 cases of lupus erythematosus, in 32 of which chest films were available, were reviewed (Table 2).

As far as anatomic sites other than those mentioned in Table 2 are concerned, radiological findings were limited. In one case hepatomegaly was reported; in two cases, ascites was noted. No gastrointestinal lesions were detected. In one case, slight osteoporosis of the hands was noted. While there was clinical evidence of joint disorder in many cases, there were no reports of roentgen studies of the joints (largely because examination was not regarded as necessary by the ward physician).

Biopsy or necropsy material compatible with the diagnosis of disseminated lupus erythematosus was available in 24 out of the 35 cases. In two cases biopsy reports were negative.

TABLE 2.—*Observations in x-ray films of the chest in 32 cases of disseminated lupus erythematosus*

No evidence of disease		11
Evidence of disease		21
Cardiac enlargement	5	
Pericardial effusion	5	
Pleural effusion	13	
Pulmonary changes	10*	

*The pulmonary changes consisted of accentuated basal bronchovascular markings in two instances, of nodular or patchy pulmonary densities (possibly edema) in six instances, and of diffuse pulmonary density (edema) in two instances.

The following are illustrative case reports:

¶ A white girl 19 years of age had facial rash of butterfly shape, fever, pain in the joints of six months' duration, and generalized edema (nephrotic syndrome?) of four weeks' duration. X-ray films of the chest showed a small amount of fluid in the costophrenic sulci. (This minimal, bilateral effusion, without other roentgen evidence of chest disease, is one of the more suggestive findings of disseminated lupus erythematosus—in patients with concomitant clinical symptoms.) Biopsy was not performed.

¶ A 13-year-old boy entered the hospital with high fever and weakness, splenomegaly and lymphadenopathy of two months' duration and a butterfly facial rash that had been present a month. Slightly accentuated pulmonary markings were noted in x-ray films of the chest. Three days later films taken at bedside showed bilateral pneumonitis, and six days later the patient died. At autopsy disseminated lupus erythematosus was observed, and also bilateral atypical lobar pneumonia with features suggesting the anaphylactic pneumonia reported by Rich[18] as occurring in rheumatic fever and in patients with sulfonamide sensitivity.

¶ A 25-year-old housewife had peripheral arthritis with migratory pain in the joints. An episode of hematuria had occurred a month before admittance to hospital, and fever and a pericardial friction rub had been present for three days. X-ray films showed some small nodular densities in

the right lower lung field, small bilateral pleural effusions and cardiac enlargement. No abnormality was noted in an intravenous pyelogram. Biopsy was not performed.

Polysystemic manifestations such as were noted in this case (articular, renal, pericardial, pulmonary), plus the small bilateral pleural effusions, are highly suggestive of a collagen disease. Cases such as the present one, in which there is no development of skin lesions during the course of disseminated lupus erythematosus, are few. In a few others the skin lesions may appear only fleetingly.

¶ A 15-year-old girl had painful, swollen joints and fever. X-ray films of the chest showed a "water-bottle" shaped heart suggesting pericardial effusion (this was confirmed by fluoroscopy). Minimal bilateral pleural effusion also was noted. Examination 18 days later showed a pronounced decrease in the size of the heart; the pleural effusions were unchanged. The clinical diagnosis was disseminated lupus erythematosus. Biopsy was not performed.

¶ The patient was a 36-year-old white man with a history of chorea at age 12. Two and one-half years before admittance to hospital, a butterfly rash developed, then hematuria and fever, weakness and fatigue. Some ten months before the x-ray and autopsy examinations reported herein were carried out, the patient was hospitalized and disseminated lupus erythematosus was diagnosed. The blood pressure at that time was 170 mm. of mercury systolic and 96 mm. diastolic. After several months, pronounced orthopnea and minimal edema developed and the blood pressure varied from 160 mm. of mercury systolic and 90 mm. diastolic to 200 mm. and 110 mm. respectively. The patient died of cardiac failure. X-ray films taken ten days before death showed cardiac enlargement. At autopsy chronic glomerular nephritis (without evidence of disseminated lupus erythematosus) and lesions of the spleen consistent with disseminated lupus erythematosus were noted. There was microscopic evidence of active rheumatic lesions. In this case there was a combination of "collagen" diseases.

Dermatomyositis

Dermatomyositis, the rarest of the collagen diseases, is characterized by non-suppurative inflammation of the skin, the subcutaneous tisssues and the skeletal muscle. There also may be inflammatory changes in the vessels, the myocardium and the muscles of deglutition. Little is known of the radiological features. In the present series there was only one autopsy-proven case, and in that case cloudy swelling of the myocardium and congestive failure was noted at necropsy. X-ray films of the chest taken a year before death showed the heart slightly larger than normal, but several weeks before death the heart-vessel shadow was normal in size. The lungs were clear.

Scleroderma

Scleroderma is a polysystemic disease, with fairly well known roentgen findings. Large series of cases have been reported in the literature, one of the most comprehensive, from the radiological viewpoint, being that by Pugh.[15] Table 3, prepared from data in the literature and the authors' observations, is believed to summarize the more important radiological changes in this disease.

TABLE 3.—*Summary of the radiological findings in scleroderma*

- A. Gastrointestinal Tract
  - 1. Esophagus
    - a. Loss of peristalsis due to rigidity
    - b. Variable degrees of dilatation
    - c. Occasional narrowing of distal esophagus
    - d. Occasional shortening of esophagus
  - 2. Stomach
    - a. Peristalsis may be decreased
    - b. Hiatus hernia may develop
  - 3. Small Bowel
    - a. Peristalsis decreased or absent
    - b. Widening, especially of duodenum and jejunum; this may be segmental
  - 4. Colon
    - a. Peristalsis decreased
    - b. Segmental narrowing
- B. Lungs
  - 1. Diffuse or localized fibrosis
  - 2. Diffuse or localized nodulation
  - 3. Subpleural "cystic disease" (basal)
  - 4. Calcification (calcinosis)
- C. Heart
  - 1. Decreased amplitude of excursion
  - 2. Heart may be small, normal or large
- D. Phalanges
  - 1. Absorption of distal phalanges in advanced cases
  - 2. Occasional increased density of phalanges
  - 3. Occasional synostosis, distal and middle phalanges
- E. Soft Tissues
  - 1. Calcinosis—fairly frequent and often accompanies phalangeal absorption
    - a. Varies from "sand" to plaques
    - b. Usually in pressure areas: fingertips, elbows, ischial tuberosities
    - c. Usually seen only where there is cutaneous sclerosis.
- F. Teeth
  - 1. Uniform widening of the periodontal spaces (reported in 7 per cent of cases)

Roentgen studies carried out in 10 microscopically proven cases of scleroderma were reviewed. In five of them there was roentgenographic evidence of some degree of small bowel abnormality. In one case, the first suggestion of scleroderma was made by one of the authors upon examination of a film of the small bowel. It is the authors' impression that the small bowel involvement often starts as a dilatation of the third portion of the duodenum, and then progresses distally. In one case, however, the changes in the bowel appeared to start with areas of narrowing. Three of the five patients with scleroderma involving the small bowel died.

One of the ten patients with proven scleroderma had pulmonary disease:

¶ A Chinese man 75 years of age had loss of weight from 150 to 116 pounds, pronounced weakness, dyspnea, edema at the ankles and a cough productive of white, frothy phlegm. The skin of the face and fingers appeared drawn, tense and shiny. The patient died of ruptured diverticulitis of the midascending colon eight days after treatment with corticotropin was started. X-ray films of the chest five months before death showed minimal prominence of the lower lobe pulmonary markings and slight cardiac enlarge-

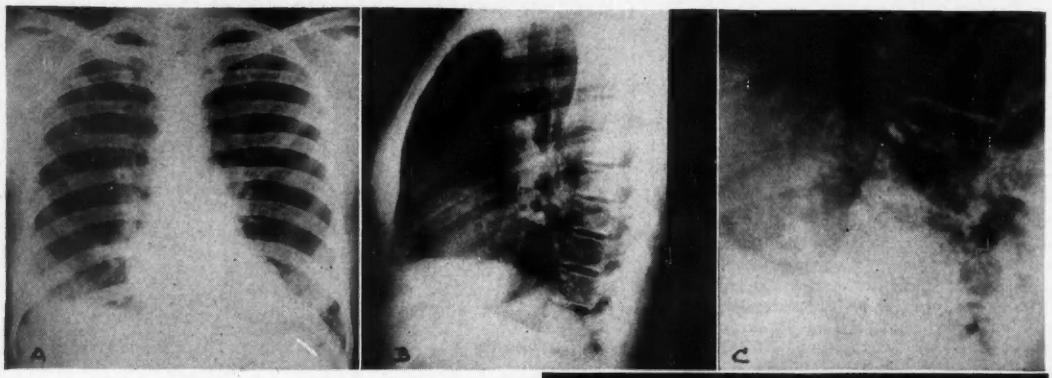
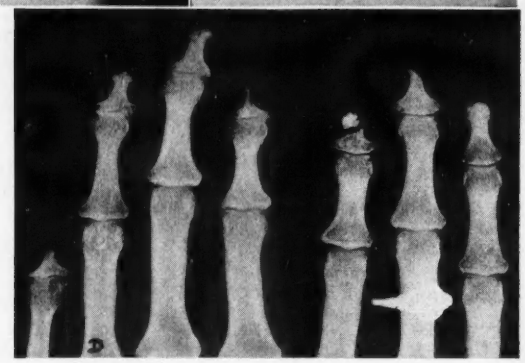


Figure 3.—Scleroderma, with cystic disease of the lung bases. The patient, a Negro woman 30 years of age, had had scleroderma for twelve years. *A*. Mottled radiolucencies (? cysts) in lung bases. *B*. Lateral view of same. *C*. Detail view of cystic appearance. *D*. Tuft absorption and calcinosis.



ment. Examination three days before corticotropin therapy was begun showed hazy widening of the pulmonary markings throughout both lung fields, with a few areas of small (2 to 3 mm.) hazy nodules along the course of these markings. The changes were more evident in the right upper lobe, where one patchy density (1.5 x 3 cm.) also was present. The left costophrenic sulcus was blunted by fluid.

Among several clinically diagnosed cases of scleroderma was one in which there were subpleural cystic changes. The patient was a Negro woman 30 years of age with definite scleroderma for 12 years. X-ray films of the chest showed a peculiar "spongy" appearance in the bases of the lungs, presumably due to cystic changes as described by Getzowa[7] in two cases. Getzowa considered the changes examples of "cystic and compact pulmonary sclerosis." The "cysts" varied from pinhead size up to 1.5 cm. in diameter. In only one of the two cases was there concomitant extensive fibrosis. The cystlike changes were believed to be due to a disappearance of alveolar tissue in the lung secondary to lysis of the alveolar walls and progressive sclerosis. This sclerosis is reportedly on the basis of "a hyaline process involving the alveolar walls, accompanied by the disappearance of capillaries, superimposed on a generalized, diffuse simple fibrosis of the alveolar walls."

Reports of other cases illustrative of features of scleroderma follow:

¶ A white woman, 42 years of age, was admitted to hospital with a history of attacks of abdominal pain, nausea, vomiting and diarrhea for about 18 months. She had had peripheral vascular changes of the Raynaud's disease type for two years. About eleven months before entry she had had cholecystectomy; chronic cholecystitis was reported.

X-ray examination revealed widening and delay in the third portion of the duodenum and proximal small bowel. Fluoroscopically, the esophagus showed sluggish passage of the barium. No abnormalities were noted in x-ray films

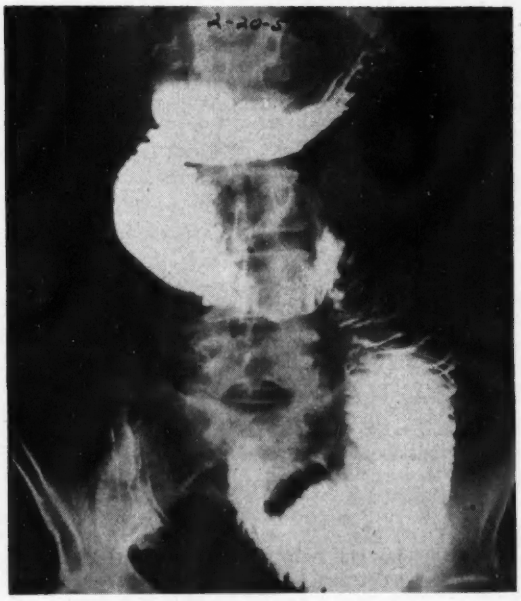


Figure 4.—Scleroderma, with involvement of small bowel. The patient was a 42-year-old white woman. Raynaud's phenomenon had been present two years. There had been attacks of abdominal pain, nausea, vomiting and diarrhea for one and one-half years. Autopsy, six months after examination, showed generalized scleroderma. X-rays showed upper small bowel dilation and delay.

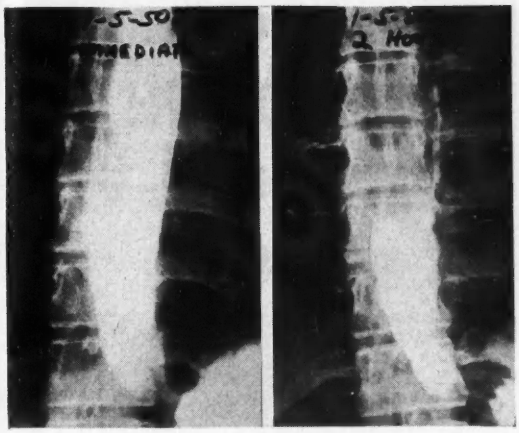


Figure 5.—Scleroderma, with esophageal involvement. The patient was a white woman 36 years of age with onset of disease three years previously, and with recent nausea, anorexia and dysphagia. Biopsy of skin showed scleroderma. X-ray examination showed esophageal widening, decreased peristalsis and pronounced delay.

of the chest and hands. Six months later the patient died "from asthenia," and at autopsy generalized scleroderma was observed.

A 36-year-old white woman had sclerodermal symptoms for three years, starting as pain and stiffness in the extremities, followed by Raynaud's phenomenon. About one month before admittance to hospital, nausea, anorexia and dysphagia occurred. X-ray examination showed esophageal involvement, with widening, decreased peristalsis and pronounced delay in emptying. A biopsy of skin showed changes interpreted as scleroderma. When the patient was observed two and one-half years later, only slow progression of the disease was shown.

A 46-year-old Greek woman had the onset of scleroderma 15 years before admittance to hospital and dysphagia had been present for twelve years. X-ray examination showed esophageal and duodenal involvement, with widening and delay in each site. Calcinosis was noted in the soft tissues of the fingertips and prepatellar areas. Changes noted in skin biopsy were interpreted as scleroderma. The general health of the patient three years later was relatively good.

Rheumatic Fever and Rheumatoid Arthritis

Acute rheumatic fever is regarded as a collagenous degeneration which localizes selectively in the heart. The changes may be found in many other organs, as shown by the arthritic, dermal, serosal, intestinal and pulmonary manifestations of the disease. In the acute fulminating form of the disease, pulmonary complications are reportedly found in as high as 50 per cent of cases.[8] "Rheumatic pneumonitis" has no specific diagnostic features in our experience. Pericarditis is not uncommon. The involved joints tend to show only articular and periarticular swelling.

Rheumatoid arthritis is frequently complicated by myositis, neuritis and arteritis, as demonstrated in 70 per cent of muscle biopsies by Traut and Campoine.[21] Traut also stated that the biopsies showed aggregates of lymphocytes, epithelioid cells and plasma cells somewhat similar to those in dermatomyositis, lupus erythematosus and scleroderma. Pericarditis is the only unusually frequent cardiac complication, being especially common in juvenile rheumatoid arthritis (Still's disease). In addition, pneumonitis and pleuritis may occur along with the inflammatory reaction in the joints, but is rare. The x-ray findings in the bones and joints of patients with rheumatoid arthritis are well known.

DISCUSSION

Collagen diseases constitute an interesting group of disorders from the clinical side because of diagnostic and therapeutic challenge, from the pathological viewpoint because of recent interest in the intercellular substances, and from the radiological viewpoint because of their widespread but unfortunately non-specific nature. The latter is particularly true of the pulmonary manifestations of the collagen diseases. The authors feel that diagnostic possibilities, slim though they are, are enhanced by an awareness of these conditions, plus a knowledge that the patient has a polysystemic disease. It is desirable that radiologists, as clinicians, be able occasionally to suggest the consideration of one of these diseases, on logical grounds, and be cognizant of the further studies, clinical, laboratory or pathological, required to confirm the diagnosis.*

From a review of radiological findings in the present series, the authors have come to believe that pulmonary changes occur more frequently in periarteritis nodosa and disseminated lupus erythematosus than one would gather from the literature. Further, a survey of the histories of over 75 patients with established or clinically diagnosed collagen disease led to the distinct impression that peptic ulcers occur with relatively greater frequency in persons with these conditions than in other patients in hospitals in general.

In studying a patient for possible collagen disease it is desirable that particular attention be paid to the following structures: The skin and muscles, the heart and pericardium, the lungs and pleura, the abdomen and intestinal tract, the kidneys, and the bones and joints.

The skin and muscles may show microscopic evidence of involvement in any of the four types of collagen disease herein discussed—periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis and scleroderma. Histopathologic changes are reportedly fairly decisive in all except dermatomyositis, about which not enough is yet known; they are

*At the same time, it is believed that the term "collagen" disease is one of high abstraction, to be modified or abandoned as soon as advances in knowledge of the cause and of the fundamental nature of these conditions permit.

said to be most clear-cut in periarteritis, but there is divergence of opinion as to the clarity of changes in scleroderma.

The cardiac and pleuropulmonary changes are legion and non-specific. Pericardial effusion, cardiac enlargement, pleural effusion, pulmonary nodular changes and variable degrees of pulmonary edema or fibrosis may occur. These changes may be reversible.

Abdominal distention, with paralytic obstruction, may occur in periarteritis nodosa and disseminated lupus erythematosus, as also may renal enlargement.

The intestinal tract changes are most conspicuous in scleroderma, notably in the esophagus and small bowel (variable degrees of rigidity, dilation and narrowing occur in about 50 per cent of cases).

The articular and osseous changes occur in periarteritis, lupus and especially scleroderma. Radiologically, they are characteristic only in the latter condition. Calcinosis is also confined largely to this disorder.

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REFERENCES

1. Barden, R. P., and Cooper, D. A.: The roentgen appearance of the chest in diseases affecting the peripheral vascular system of the lungs, Radiology, 51:44-57, July 1948.

2. Becker, R. M.: Hypersensitivity and diffuse vascular (collagen) diseases, Bull. New Eng. Med. Center, 11:127-133, June 1949.

3. Editorial, J.A.M.A., 150:220-221, Sept. 20, 1952.

4. Ehrick, W. E., Forman, C., and Seifter, J.: Experimental differentiation of pathogenesis of serum sickness, glomerular nephritis, rheumatic fever, and periarteritis nodosa, Am. J. Med. Sci., 215:713, 1948.

5. Elkeles, A., and Glynn, L. E.: Serial roentgenograms of chest in periarteritis nodosa as an aid to diagnosis, with notes on pathology of pulmonary lesions, Brit. J. Rad., 17: 368-372, Dec. 1944.

6. Foldes, J.: Acute systemic lupus erythematosus, Am. J. Clin. Path., 16:160-173, March 1946.

7. Getzowa, S.: Cystic and compact pulmonary sclerosis in progressive scleroderma, Am. J. Path., 21:25-41, 1945.

8. Griffith, G. C., Phillips, A. W., and Asher, C.: Pneumonitis occurring in rheumatic fever, Am. J. Med. Sci., 212:22-30, July 1946.

9. Hargraves, M. M., Richmond, H., and Morton, R.: Presentation of two bone marrow elements: The "tart" cell and the "L.E." cell, Proc. Staff Meeting, Mayo Clinic, 23:26, 1948.

10. Kampmeier, R. H.: Vascular diseases due to hypersensitivity: So-called diffuse collagen disease, Am. Prac., 1: 113, 1950.

11. Klemperer, P., and others: Cytochemical changes of acute lupus erythematosus, Arch. Path., 49:503-516, May 1950.

12. Libman, E., and Sacks, B.: A hitherto undescribed form of valvular and mural endocarditis, Arch. Int. Med., 33:701, June 1924.

13. Logue, R. B., and Mullins, F.: Polyarteritis nodosa: Report of eleven cases with review of recent literature, Ann. Int. Med., 24:11-26, Jan. 1946.

14. Miale, J. B.: Characteristic urinary sediment in visceral angiitis, Am. J. Clin. Path., 17:820-822, Oct. 1947.

15. Pugh, D. B.: Roentgenologic manifestations of scleroderma, Am. J. Med. Sci., 216:571-580, Nov. 1948.

16. Rakov, H., and Taylor, J. S.: Acute disseminated lupus erythematosus without cutaneous manifestations and with heretofore undescribed pulmonary lesions, Arch. Int. Med., 70:88-100, July 1942.

17. Reeder, W. H., and Goodrich, B. G.: Pulmonary infiltration with eosinophilia (PIE syndrome), Ann. Int. Med., 36:1217-1240, 1952.

18. Rich, A. R., and Gregory, J. E.: On the anaphylactic nature of rheumatic pneumonitis, Bull. Johns Hopkins Hosp., 73:465-470, 1943.

19. Stewart, L. L. as quoted by R. W. Hollenhurst and J. W. Henderson: The ocular manifestations of the diffuse collagen diseases, Am. J. Med. Sci., 221:211-222, Feb. 1951.

20. Thorell, I.: Pulmonary changes in cases of disseminated lupus erythematosus, Acta Rad., 37:8-11, Jan. 1952.

21. Traut, E. F.: Rheumatic Diseases, C. V. Mosby Co., St. Louis, 1952.

Swallowed Foreign Bodies

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• *Of 98 swallowed foreign bodies demonstrated, 71 with fate definitely known are reported. Seventeen of 20 foreign bodies in the esophagus had esophagoscopic removal. Only two of 51 foreign bodies in the gastrointestinal tract had laparotomy, while 49 were spontaneously passed.*

Early esophagoscopic removal of foreign bodies lodged in the esophagus and conservative management of foreign bodies which have passed the esophagogastric junction are recommended. Laparotomy is rarely indicated in the management of swallowed foreign bodies, although various observers are not in full agreement as to the circumstances in which "watchful waiting" is advisable nor as to how long it is permissible to wait for spontaneous passage.

In 20 of 71 cases of swallowed foreign bodies, the objects were in the esophagus at the time the patient was first examined. Esophagoscopic removal was carried out in 17 cases. In two cases a foreign body was passed per rectum and in one was vomited. Laparotomy for removal was done in only two of the 51 cases in which the foreign body was already in the stomach or bowel at the time of examination, and in one of them the operation probably could have been avoided.

IN MOST CASES a swallowed foreign body gets by the esophagogastric junction and is passed spontaneously by rectum, but if it lodges in the esophagus early esophagoscopic removal usually is necessary.

Since the Los Angeles County Harbor General Hospital has an active emergency receiving service and draws from a fairly representative surrounding community, it was felt that the cases of swallowed foreign bodies that were encountered there might be fairly representative of those likely to be seen by the average practitioner. In a period of three and a half years 195 patients with complaint of having swallowed a foreign body were observed there, and in 98 instances the presence of a foreign body was unequivocally demonstrated either radiographically or by recovery in the stool or by esophagoscopic operation. However, information is complete in only 71 of the cases and the present report therefore is limited to that group.

The foreign bodies swallowed showed considerable variation in size and shape. There were about as many dull objects as there were sharp (Table 1).

The ages of the patients ranged from 2 months to 85 years. Twelve were under one year of age, but more than half were in the 1- to 4-year group. Bone fragments were more common in the elderly patients, particularly in those who wore false teeth (see Table 2).

FOREIGN BODIES IN THE ESOPHAGUS

Twenty of the 71 foreign bodies were lodged in the esophagus. Seventeen of the 20—6 bony fragments, 2 open safety-pins, 7 coins, 1 ring and 1 chunk of meat—were removed at esophagoscopy after periods of from 1 to 72 hours. Of the 3 foreign bodies not removed at esophagoscopy, one, a large hairpin in the cervical esophagus, was spontaneously vomited and the other two were passed by rectum. One, the end of a toy horn, was lodged in the distal esophagus for several hours and then spontaneously passed in the stool the next day. The other, a penny, was apparently pushed into the stomach at esophagoscopy and then passed uneventfully (see Table 3).

Foreign bodies lodged in the esophagus may be of serious consequence. They may occasionally pass spontaneously into the stomach or rarely be vomited. But as a rule if the foreign body is shown in roentgen examination to be lodged high in the esophagus, early esophagoscopy is indicated. If it is low in the esophagus haste is not imperative, although watchful waiting should generally not be extended beyond 24 hours. The longer the delay the greater the likelihood of increasing edema with consequent greater difficulty in removal at esophagoscopy.

In the pharynx and esophagus flat foreign bodies such as coins become lodged so that they are seen *en face* in frontal projections, and on edge in lateral projections (see Figure 1). The reverse is generally true when such objects are lodged in the trachea.

FOREIGN BODIES IN THE GASTROINTESTINAL TRACT

Of the 51 foreign bodies that had gotten by the esophagogastric junction all but three passed spon-

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TABLE 1.—*Types of foreign bodies*

Dull		Sharp	
Coins	25	Bones (fish and fowl)	10
Metal tipped eraser	1	Nail	8
Metal nut	3	Bobby pin	5
Marble	2	Straight pin	5
Bolt	2	Tack	7
Clothes-pin spring	1	Glass	2
Extracted tooth	1	Hairpin	2
Gold tooth filling	2	Open safety-pin	4
Hair barrette	1	Screw	1
Metal cylinder	1	Corsage pin	1
Paper clip	1	Needle point	1
Metal whistle	1	Phonograph needle	2
Clock winding key	1	Steel shaving	1
Suspender clip	1		
Closed safety-pin	2	Total	49
Metal knob	1		
Metal rivet	1		
Metal button	1		
Ring	1		
Meat chunk	1		
Total	50		

TABLE 2.—*Age of patient and type of swallowed object*

Age	Dull Objects: Coins	Dull Objects: Other	Sharp Objects: Bones	Sharp Objects: Other	Total: No.	Total: Pct.
Under 1 year	5	3	....	4	12	12
1 to 4 years	18	17	1	18	54	55
5 to 9 years	2	1	1	7	11	11
10 to 14 years	....	....	....	4	4	4
15 to 85 years	....	4	8	6	18	18
Total cases	25	25	10	39	99	100

TABLE 3.—*Delivery of swallowed objects from esophagus*

	Dull Objects: Coins	Dull Objects: Other	Sharp Objects: Bones	Sharp Objects: Other	Total: No	Total: Pct.
Passed per rectum	1	1	....	....	2	10
Removed by esophagoscope	7	2	6	2	17	85
Vomited	....	....	....	1	1	5
Total cases	8	3	6	3	20	100

TABLE 4.—*Delivery of swallowed objects from gastrointestinal tract*

	Dull Objects: Coins	Dull Objects: Other	Sharp Objects: Bones	Sharp Objects: Other	Total: No	Total: Pct.
Spontaneously passed per rectum	10	13	....	25	48	94
Removed by laparotomy	....	....	....	2	2	4
Removed from rectum by manipulation	....	....	1	....	1	2
Total cases	10	13	1	27	51	100

taneously. One of the three that did not, a chicken bone, lodged in the rectum and manual removal was necessary. In the other two instances laparotomy was carried out. The objects spontaneously passed were 18 coins, 3 bone fragments, 7 nails, 5 bobby-pins, 5 straight pins, 2 open safety-pins, 1 6 cm. corsage pin, and several assorted metallic and plastic objects (see Table 4).

Following are reports of the two cases in which laparotomy was done:

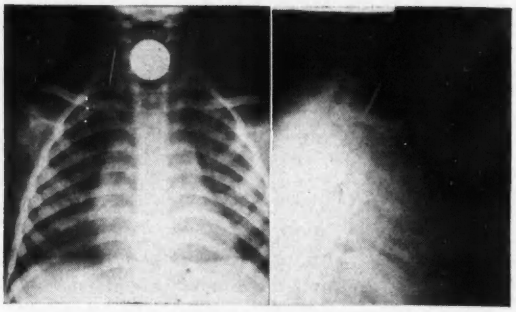

Figure 1.—Coin lodged in the cervical esophagus.

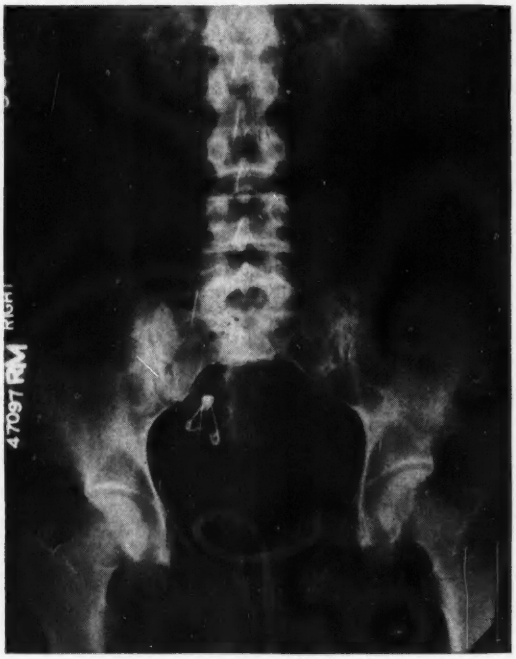

Figure 2.—Two safety-pins in the distal ileum, stationary about 10 hours. They were closed through the wall of the bowel at laparotomy (the operation probably need not have been done), and subsequently passed.

Case 1. A 26-year-old white woman "accidentally" swallowed three open safety-pins. One lodged in the cervical esophagus and was removed at esophagoscopy about 16 hours after ingestion. The other two reached the region of the ileocecal valve. There, appearing to interlock (Figure 2) they remained stationary for about 10 hours. Although there were no untoward symptoms, laparotomy was done. The pins were found freely movable in the terminal ileum. They were closed through the intestinal wall and "milked" to the hepatic flexure. The bowel was not opened. The pins were passed per rectum. The patient was subsequently returned to the hospital on several occasions for attempted suicide.

In retrospect it seems that laparotomy was probably not indicated at that time and could have been delayed for at least an additional 48 hours of conservative management and several weeks if necessary.

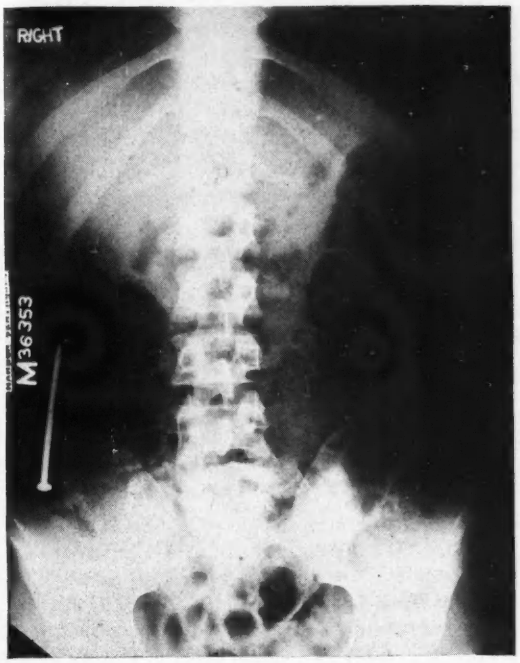

Figure 3.—A 9 cm. tenpenny nail perforating the cecum. It was removed at laparotomy four years after ingestion.

CASE 2. A 26-year-old white man was admitted to hospital with symptoms consistent with acute appendicitis. However, in a plain film of the abdomen a 9 cm. tenpenny nail was seen in the right lower quadrant. Upon questioning, the patient admitted swallowing the nail four years previously, just before going to prison, in order that he might have a weapon while incarcerated. Although the nail was not passed as expected, it caused no symptoms until the present illness. Upon operation, the nail was found to be perforating the lateral wall of the cecum and lying in the lateral gutter with the point cephalad. Only the head of the nail was still intraluminal. The appendix appeared normal. The postoperative course was uneventful and the patient was discharged ten days after operation.

In this, the only case in the series in which laparotomy was definitely indicated for removal of a foreign body from the gastrointestinal tract, there were no serious consequences directly attributable to the long delay.

Foreign bodies that have entered the stomach will as a rule pass uneventfully through the gastrointestinal tract. It may take longer for large and pointed objects to pass, but rarely is laparotomy necessary.

DISCUSSION

While there are differences of opinion as to the amount of "watchful waiting" that is indicated in dealing with swallowed foreign bodies, most observers agree that conservative management is in order. Best[2] stated: "As a rule, those who have had the greatest experience in the management of such cases advocate careful observation and non-surgical treatment, while those with only an isolated experience tend to favor surgical interference."

The initial roentgen examination to establish whether a foreign body is present generally consists of three films, although fewer may suffice. These are a lateral view of the neck, a lateral view of the chest and an anteroposterior view of the abdomen. If these views do not reveal a foreign body and the history suggests that it may not be radiopaque, the lateral films of the neck and chest should be repeated after a swallow of thick barium. The barium shadow may give evidence of an obstruction or the material may adhere to a relatively radiolucent object and thus render it visible. If a foreign body is not demonstrated by these simple means, fluoroscopy with the swallowing of barium-soaked cotton pledgets or barium capsules may be effective, but as a rule, in the authors' experience, these additional procedures are disappointing. Careful barium study of the gastrointestinal tract may occasionally reveal an otherwise overlooked radiolucent foreign body that lies below the esophagogastric junction.

Brown[3] described in detail the roentgen findings in cases of esophageal foreign bodies, particularly those in which they are lodged in the cervical esophagus. He was of the opinion that if the width of the retrotracheal space exceeds that of the trachea or vertebral bodies the presence of a foreign body should be suspected even in the absence of a radiopaque shadow.

The authors agree with Grekin and Musselman[11] that prompt action is indicated if a foreign body is above the cricopharyngeal ring when first observed, for at that level it can be relatively easily removed through an esophagoscope, whereas with delay it may become lodged farther down the esophagus and be more difficult to remove. Should the foreign body be below the cricopharyngeal ring, a few hours of observation may be permissible in the hope that it will enter the stomach; but if it does not progress in 12 to 24 hours, esophagoscopic removal is urgently indicated. Further delay only results in increasing edema and firmer impaction, and necrosis and perforation become more likely.

Esophagoscopy may be advisable if symptoms persist for more than a day, even though a foreign body is not roentgenographically visible, for it may be that the symptoms are caused by a radiolucent object.

When a foreign body lies below the esophagogastric junction, watchful waiting is proper. Taking a single plain film of the abdomen daily for the first few days and then every other day if progression is slow but definite, will usually suffice. A regular diet

without excessive roughage is advisable. Catharsis is contraindicated.

Observers differ as to how long a foreign body may remain stationary before surgical intervention is justified. Chambers,[6] who reported upon 16 cases in prison inmates who were sent to the hospital because of intentional swallowing of foreign bodies, said: "In general, six weeks may be taken as a rough guide to the period a foreign body which is producing no symptoms may be left in situ." Grekin and Musselman,[11] who reported upon 59 cases, placed the period at four weeks. Woodburn,[15] in a report on 50 cases in children, expressed the opinion that if a foreign body, particularly if sharp, remains at one level for more than five days, operation should be done; and Best[2] who reported on 12 cases in which sharp-pointed foreign bodies were deliberately swallowed in a disciplinary center, felt that laparotomy should be carried out if a sharp object is arrested at site for more than 48 hours.

The size and shape of a foreign body of course must influence estimates of the likelihood of passage, and hence the indications for laparotomy. However, it is generally agreed that signs of perforation, obstruction or hemorrhage are indications for immediate operation. Although large, pointed or jagged foreign bodies do not always cause perforation, in most cases in which perforation does occur the foreign body is of that kind.

McManus,[12] in a review of reports of 93 cases in which perforation occurred, noted that in 45 per cent of cases the foreign bodies were pins, bits of wire and similar objects, in 45 per cent bones, and in 10 per cent toothpicks and wood splinters. The perforations were in the lower ileal and cecal regions in 63 per cent of cases, and in one third of cases the perforation was at the appendix.

Perforation occurred in only one case in the present series (reported in a preceding paragraph) and in other cases such objects as open safety-pins, hairpins and a 6 cm. corsage pin (Figure 4) were passed uneventfully, the latter in two days.

Exner[8] demonstrated the remarkable ability of the intestine to protect itself against perforation. He introduced sharply pointed objects, point first, into the intestinal tract of animals. Almost invariably these objects were expelled with their points trailing rather than leading. To learn by what mechanism the reversal was brought about, Exner gently pricked the intestinal mucosa of animals with sharply pointed objects and noted that an area of ischemia with a large central concavity developed at the site. Thus, pricking the bowel wall increases the lumen of the bowel at the point of contact, permitting freer progress to the offending object.

It is probable that in many cases swallowed foreign bodies pass through the gastrointestinal tract without causing symptoms and a physician is not consulted. In one case in the present series, that of a 2-year-old child, a small metal cylinder was incidentally noted in the gastrointestinal tract on films taken because it was thought the patient might have a fracture of the lumbar spine. The foreign body was uneventfully passed within two days.

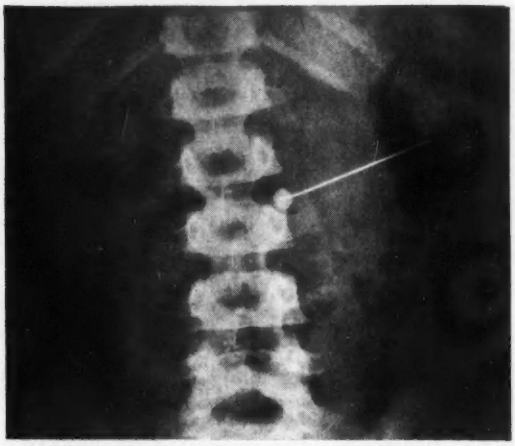

Figure 4.—A 6 cm. corsage pin swallowed by a 5-year-old. Passed spontaneously.

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REFERENCES

1. Benedict, E. B.: Vomiting of an open safety-pin, N.E.J.M., 230:484, April 20, 1944.

2. Best, R. R.: Management of sharp-pointed foreign bodies in the gastrointestinal tract, Am. J. Surg., 52:545-549, Oct. 1946.

3. Brown, S.: Foreign bodies in the digestive tract, Radiology, 44:143-150, Feb. 1945.

4. Carp, L.: Foreign bodies in the intestine, Ann. Surg., 85:575-591, April 1927.

5. Carp, L.: Foreign bodies in the gastrointestinal tract of psychotic patients, Arch. Surg., 60:1055-1075, June 1950.

6. Chambers, G. O.: Foreign bodies in the alimentary tract, Brit. Med. J., 4624:362-365, Sept. 26, 1942.

7. Delaney, C. J.: Foreign bodies swallowed by children, N. Y. State J. Med., 40:1024-1026, July 1, 1940.

8. Exner, A.: Wie schuetzt sich der verdanungstract ver verletzungen durch spitze fremdkoerper, Arch. f.d. ges physiol., 89:253, 1902.

9. Flett, R. L.: Oesophageal foreign bodies and their complications, J. Laryng. and Otol., 60:1-15, Jan. 1945.

10. Friedberg, S. A.: Esophageal foreign body with symptoms suggesting other thoracic disease, Arch. of Otolaryng., 34:591-592, Sept. 1941.

11. Grekin, T. D. and Musselman, M. M.: Management of foreign bodies in the alimentary tract, Ann. Surg., 135:528-535, April 1952.

12. McManus, J. E.: Perforation of the intestine by ingested foreign bodies, Am. J. Surg., 53:393-402, Sept. 1941.

13. Persky, L., and Frank, E. D.: Foreign body perforation of the gastrointestinal tract, N.E.J.M., 246:223-224, Feb. 7, 1952.

14. Weintrob, M., and Granet, E.: Management of swallowed sharp foreign bodies, J. Internat. Coll. Surg., 8:459-469. Sept.-Oct. 1945.

15. Woodburn, J. W.: Foreign bodies in the food passages of children, Med. J. of Australia, 2:15-16, July 1, 1950.

Progressive Muscular Dystrophy

A Preliminary Report on Treatment with Amino Acids, Folic Acid and Vitamins

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• Ten patients with progressive muscular dystrophy were given daily oral doses of amino acids, folic acid and selected vitamins.

At the time of this report they had been treated by this means for periods varying from two months to one year. Only one had other therapy concurrently.

Definite and progressive improvement, objective and subjective, occurred in all cases. Among objective changes noted—not all of them in all cases—were return of strength, increase in size and tonus of atrophic muscles, restoration of normal respiratory action and relief of depression. Patients reported a sense of well-being, increase in strength and a feeling of bodily warmth.

TEN CONSECUTIVE unselected patients with progressive muscular dystrophy were given amino acids, folic acid and selected vitamins on the assumption that the wasting process in the muscle is secondary either to failure of the digestive system to split the protein molecule into the basic amino acids or to a disorder of the enzymatic system for the synthesis of muscle tissue.

The patients, six females and four males ranging in age from 6 to 51 years, were first examined in the outpatient neurological clinic of the University of California School of Medicine, San Francisco, and were then admitted to hospital for diagnostic procedures including muscle biopsy, creatine and creatinine studies, determination of muscle strength and, in some cases, electromyographic examination. All had progressive muscular dystrophy.

The three classical types of muscular dystrophy —Erb's juvenile, fascioscapulohumoral, and pseudohypertrophic—were represented. Some of the patients had had various forms of therapy previously without arrest of progression.

Each patient was given daily:

†	Vitamin B_{12}	50.0 micrograms
	Folic acid	3.34 mg.

and a proprietary protein hydrolysate* mixture that, in the amounts given, contained approximately:

Amino acid produced by enzymatic digest of casein	16.0	gm.
Ascorbic acid	100.0	mg.
Thiamine hydrochloride	10.0	mg.
Riboflavin	6.0	mg.
Pyridoxine hydrochloride	1.0	mg.
Calcium pantothenate	1.0	mg.
Niacinamide	50.0	mg.
Vitamin A	5,000	USP units
Vitamin D	500	USP units
Iron peptonate	0.1	gm.
Tribasic calcium phosphate	1.0	gm.

Directions were given to take one heaping teaspoonful of the protein hydrolysate mixture, mixed with liquids or solid food, with meals three times a day. One capsule of B_{12} and folic acid was taken morning and evening.

The patients were requested to make no change in their mode of living. With one exception, none received any other therapy concomitantly. Each patient kept a written, chronological record of any changes in physical status and of reactions to the regimen. Suggestions of any kind that could influence the patient were strictly avoided.

At the time of this report the patients had been treated by this means for periods varying from two months to one year. Definite and progressive improvement, objective and subjective, occurred in all cases. All the patients gained strength. In some cases atrophic muscles that had minimal contractility and no measurable function before treatment, developed power and returned to approximately normal size.

Common subjective reactions were reported as follows: A few days after starting treatment, patients experienced a sense of generalized warmth. Previously they had always felt cold. Some patients thought they had fever, but normal temperature prevailed. A sense of well-being usually developed concomitantly. After about ten days of treatment, many had a feeling of "fullness" in the head, and some described it as a continuous dull throbbing headache. This lasted from a few days to approximately

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†Rubrafolin capsules (folic acid and vitamin B_{12}) were supplied by E. R. Squibb and Sons, New York.

*Walker's Protein Hydrolysate with vitamins and minerals was supplied by the Walker Laboratories, Inc., of Mount Vernon, N. Y.

two weeks and did not recur. Some reported muscular cramping especially in the gastrocnemius and in intrinsic muscles of the feet. This surprised them, for they had not had muscle cramps since weakness had first developed. Within three weeks to one month after the beginning of treatment a subjective sense of well-being increased and strength developed. All the patients were cheerful and gained confidence. Relatives and friends reported them to be less irritable. The improvement continued after the first month and was manifest in the ability to carry out more activity progressively with less fatigue.

CASE REPORTS

CASE 1: A woman 32 years of age had had onset of muscular dystrophy at about age 12. The muscles of facial expression were so weak that the eyes could not be closed; the mouth appeared as the typical straight line; the nasolabial folds had disappeared. Hypoventilation had resulted in a chronic cough. The patient could not raise her arms to arrange her hair, was unable to rise from a chair, and when reclining could not get up without "climbing up on herself" or using nearby objects for aid. She could not climb stairs. There was bilateral wrist drop and foot-drop on the right. The patient considered herself a complete invalid.

After treatment for one year there was complete restoration of function of the facial muscles and the chronic cough had disappeared. The patient could raise her arms with good strength (the right arm was limited, owing to winged scapula, but function was constantly improving). The strength in the forearms was normal. Foot-drop was not present and the formerly atrophic muscles were of good tonus, firm to palpation, and showing strength. The patient performed all the household duties—laundry, ironing and cooking—for a family of four and said she did not tire except on occasions of extreme and prolonged exertion. She could stand with arms extended and could flex the knees to a complete squat and then rise without assistance. She ran up a flight of stairs at the clinic.

CASE 2: The patient, a 29-year-old woman, had onset of muscular dystrophy when 13 years of age. Three sisters also had the disease, of the Erb type. The patient walked with typical gait, had exaggerated lumbar lordosis, and was unable to raise her arms above the horizontal plane. She climbed stairs with great effort, leading always with the same foot, and only if assisted or holding a hand rail. She could not lift objects by flexing her forearm. There was pronounced wasting of the gluteal muscles. The patient was depressed.

After 11 months of treatment the lumbar lordosis was less pronounced and the gait was improved. The muscles of the thigh were increased in size, were of good tonus and strength, and were firm to palpation. The patient could lift objects with flexion of the forearm and was able to care for her hair. She climbed stairs unassisted (although using the hand rail) and stepped with each leg alternately. She was cheerful and optimistic.

CASE 3: A man 51 years of age who had had muscular dystrophy for 13 years had weakness and moderate atrophy of shoulder muscles and chronic cough owing to weakness of the muscles of respiration. He became fatigued quickly on walking.

After four months of treatment, respiration was improved, coughing diminished and muscular strength increased. The patient remained critical of the treatment, but said he was able to be more active and that he tired less quickly.

CASE 4: The patient, a 39-year-old man (a brother of the patient in Case 1) had muscular dystrophy of the fasciscapulohumoral type. Onset had occurred when he was about 14 years of age. He could not rise from a supine or from a normal sitting position without assistance. The gait was fair if he was supported by someone. The patient could not raise his arms or extend his hands from the wrists. Chronic cough was present owing to weakness of the muscles of respiration.

Four months after beginning of treatment, pronounced increase in strength was noted. The hypothenar muscles were increased in size and strength. The patient could extend his hands upon the wrists. Without assistance he rose from a supine position and put his legs over the side of the bed. He could breathe deeply.

The patient reported a sense of bodily warmth and returning strength: "If I were as strong as I feel, I'd be able to do anything. I have a feeling for the first time since my illness began that I am getting better."

CASE 5: A woman 24 years of age with muscular dystrophy of Erb's type that had begun some 15 years previously, had weakness and atrophy of the muscles of the shoulder girdles. She could not rise from a chair without using her arms, and was unable to flex her forearms when carrying small objects. Climbing stairs she used the hand rail, rose always from the same foot and paused after each step to prepare for the next.

After two months of treatment she walked up seven steps with six-inch risers, rising from the right and left legs alternately and not using a hand rail. After four months she was able to rise from a chair with minimal use of her arms and could lift several dishes at a time with flexion of the forearm. She carried a quart thermos bottle of coffee, holding it upright in her hand, for several hundred feet without fatigue. Previously she could carry the bottle only by grasping it at the top and allowing her arm to hang at her side.

CASE 6: The patient, a six-year-old boy, had typically pseudohypertrophic muscular dystrophy. Onset had occurred at about age 3 and the disease was progressive. There was history of the disease in other members of the family. The patient walked with awkward gait, fell frequently, and could not stoop to pick up objects. He could be held in the forward flexed position by the pressure of one of the examiner's fingers.

After two months of therapy, strength and function were considerably improved. His mother reported: "I went to the playground to call him home. Ordinarily I could pick him out of the group as his walk was so typical, and he always trailed the group in any activity. On this occasion I did not see him, so I called his name. A youngster started running toward me, and I did not recognize my son until he came close and spoke to me. He was running and playing as normally as the other children."

The patient could rise from the prone position without the use of his hands. Considerable pressure was needed to hold him in the forward flexed position.

At last report he was able to use roller skates.

CASE 7: A sister of the patient in Case 6, eight years of age, had muscular dystrophy of pseudohypertrophic type that had begun at age 5. Her handicaps were of the same nature as her brother's but of lesser degree. She could not play active games.

After two months of treatment she carried on a full and

active program of play. The gait appeared normal, and the patient could rise from the sitting or lying position without using her hands. She could use roller skates.

CASE 8: A woman 33 years of age had muscular dystrophy of the Erb's type that had begun at about the age of 20 and for the preceding year had progressed rapidly. She could not rise from a chair, step up on a curb or board a bus without assistance. She became fatigued very rapidly and was depressed and tearful.

After treatment for two months she reported that she had climbed four steps in a normal manner, could walk well on the street, and could step up on a curb or board a bus unassisted. She was cheerful and optimistic.

CASE 9: The patient, a boy nine years of age, with muscular dystrophy of the pseudohypertrophic type, walked with a gait typical of the disease and was unable to rise from a lying or sitting posture without "climbing on himself" or on nearby objects. Signs of the disease had been present at birth. The patient was receiving physical therapy and rehabilitation therapy but the progression of weakness was not abated.

A severe attack of asthma interrupted treatment during the first month and it was begun again when the asthma subsided. During the second month of treatment (the previous program of physical therapy and rehabilitation exercise being continued concurrently) asthma did not recur, and the patient became stronger and performed movements more rapidly.

One of the exercises required of the patient in the rehabilitation therapy was to rise from a supine position on an inclined plane to a sitting position. Before therapy with amino acids, folic acid and vitamins was begun he could rise only if the plane was raised to a 22-degree slant. After two months of therapy he was able to rise from a 10-degree slant. He was able to be more active with less fatigue.

CASE 10: A woman 42 years of age had muscular dystrophy of Erb's type that had begun about 20 years previously and for the most recent three years had progressed rapidly. Following an upper respiratory tract infection in January 1953, she had remained totally incapacitated. She was unable to turn over in bed unassisted. When she was propped in a sitting position, if inadvertently her head was hyperextended on the cervical spine beyond the center of gravity, it would fall backward and the patient was unable to return it to an upright position unassisted. She had little use of her hands and no useful function in her arms. Her legs were so weak she could not stand.

After four months of therapy she could move readily in bed unassisted, could move her head freely in all directions and could bend her neck back and forth to the extremes of flexion and extension without feeling weakness or fatigue. Able to use a fork, she could feed herself while in a sitting position. At last report she could sit up without being propped and was able to stand unsupported for a few moments.

Veratrum Viride

Hypotensive and Cardiac Effects of Intravenous Use

STEPHEN R. ELEK, M.D., J. DOUGLAS McNAIR, M.D., and GEORGE C. GRIFFITH, M.D., Los Angeles

• The hypotensive action of veratrum viride given intravenously was studied in 24 patients, 22 of them hypertensive and 2 normotensive. Vasodepression of considerable but variable degree was obtained in all patients. Maximum hypotension occurred 8 to 15 minutes after injection and relative hypotension usually lasted at least two hours.

In four patients subnormal hypotension occurred but there were no clinical manifestations of shock. The blood pressure rose promptly when pressor drugs were administered.

A dose of 0.3 to 0.5 mg. brought about a satisfactory decrease in blood pressure. The degree of decrease was affected by the speed of administration and in a few patients by idiosyncratic sensitivity to the drug.

Veratrum has an extravagal action on the pulse rate, and in that and other respects resembles digitalis. Veratrum should be given with caution to digitalized patients.

Atropine reduced but did not abolish the hypotensive effect of veratrum, and was more effective when given before veratrum. This indicates that the parasympathomimetic action of veratrum is important in the mechanism of blood pressure reduction.

RECENT CLINICAL and experimental studies have renewed interest in the use of the veratrum alkaloids in the treatment of hypertension. Until a few years ago this drug was used chiefly by obstetricians in the management of eclampsia to reduce blood pressure.[5] The physiologic actions of the drug, however, were poorly known. Recent observations by Freis and co-workers[9] showed that the drug acts primarily as a vasodilator, as indicated by relatively normal flow of blood through major vascular circuits (notably the renal, hepatoportal, and muscular areas) in the presence of reduced systolic and diastolic systemic blood pressure. The peripheral vasodilation typically followed rather than accompanied the initial hypotensive action of the veratrum alkaloids, which suggested decreased total peripheral resistance.

Sympathetic vasoconstrictor reflexes are not blocked by veratrum, since vasopressor overshoots are intact and postural hypotension usually does not occur. In addition, pressor drugs such as epinephrine reverse the vasodepression produced by a mixture of veratrum viride. The oral preparations have also been reported to reverse the strain pattern in the electrocardiogram and to lower the blood pressure in hypertension.[10] McNair and co-workers[15] and Barrow and Sikes,[3] however, were not able to confirm the hypotensive effect in ambulatory patients.

The concept of vagal reflex vasodepression from veratrum is based on experimental evidence. Von Bezold and Hirt[4] and Jarisch and Richter[12] observed vasodepression and bradycardia which was abolished by sectioning the vagi; this is termed the Bezold effect. Jarisch and Richter[12] and Richter and Amann[17] further suggested that the major afferent arc of this reflex originated in the myocardium and was carried by the vagus nerve. Evidence for this was obtained by the demonstration of active afferent fibers in the cardiac branches of the vagus nerve.[1, 13] By pharmacologic methods Dawes[7] showed that the receptor area for this reflex in cats and dogs was in the left ventricle.

The efferent pathways for the Bezold reflex are incompletely known. Krayer and Acheson[14] showed in cross transfusion experiments that the peripheral vasodilation associated with the decrease in blood pressure is of neurogenic origin rather than a direct action of the drug on the arterioles. Recently Meilman and Krayer[16] noted in man that significant hypotension resulted from the intravenous administration of two of the veratrum alkaloids (protoveratrine and veratridine).

The present report is upon results of investigation of the effects of the intravenous injection of a veratrum preparation on hypertension.

PATIENTS AND MATERIALS

When this investigation was begun, the purified alkaloids of veratrum were not available; hence Veratrone® was used. It is an alcoholic solution of

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the mixed alkaloids of veratrum viride, each cubic centimeter containing 2.5 mg. of the alkaloids. The dose of Veratrone to be used was measured with a tuberculin syringe, diluted with physiological saline solution to 1.0 cc., and given intravenously in 2 to 3 minutes.

Twenty-four patients from 29 to 66 years of age were selected for study. All but three were men and most of them had a history of essential hypertension of at least five years' duration. Twenty-one patients had blood pressure of more than 150 mm. of mercury systolic and 100 mm. diastolic, one had blood pressure of 150 mm. and 90 mm. respectively, with a previously established diagnosis of chronic essential hypertension, and two patients were normotensive.

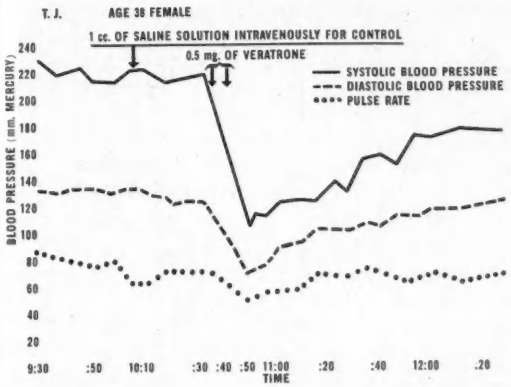

Chart 1.—Typical effect on blood pressure and pulse rate of intravenous adminstration of 0.5 mg. of Veratrone.

The patients were recumbent during the experiments and were allowed at least 30 minutes of rest for stabilization of their blood pressures before the administration of the drug. The blood pressure determinations were done with a mercury sphygmomanometer. To observe electrocardiographic changes, frequent tracings were made with a Sanborn Visocardiette. In eight of the subjects, a control injection of 1.0 cc. of normal saline solution was given intravenously before the veratrum without effect on the blood pressure or electrocardiogram.

RESULTS

1. *Hypotensive Action*

In 29 experiments on 22 hypertensive and two normotensive patients, injection of veratrum produced a significant drop in blood pressure. The usual response shown in 1 patient is recorded graphically in Chart 1 and in 5 other patients in Chart 2. These 6 patients received only 0.5 mg. of the drug, irrespec-

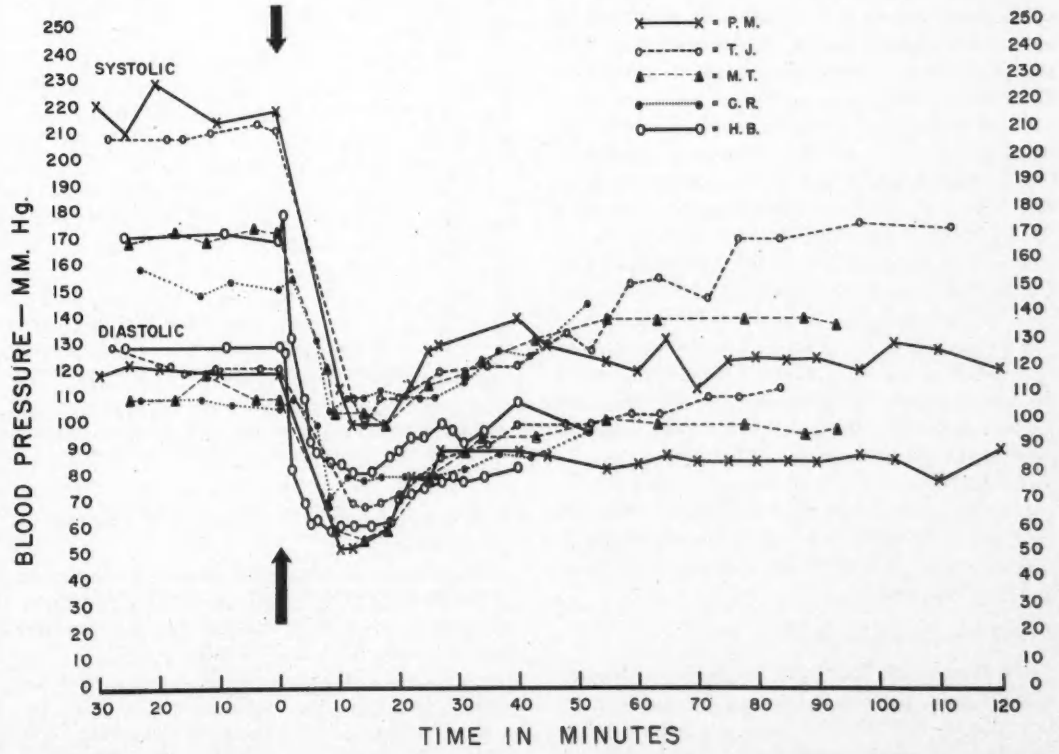

Chart 2.—Magnitude and duration of hypotensive response in five patients following intravenous injection of 0.5 mg. of Veratrone. Discussed in text.

TABLE 1.—*Data on four patients with most pronounced hypotensive response to veratrum viride.*

Case	Age	Before Injection: Blood Pressure (mm. Mercury) systolic/diastolic	Before Injection: Pulse Rate	Veratrum Dose (mg.)	Lowest Blood Pressure	Time (Minutes After Injection)	Pulse	Comment
E.G.	58	211/132	90	0.5	60/50	14	60	Rose to 110/75 19 minutes after vasopressor drug.
D.G.	65	250/170	96	0.75	116/70	12	60	Rose to 150/82 26 minutes after vasopressor drug.
H.B.	32	170/130	84	0.5	85/62	12	56	Rose to 100/78 27 minutes after vasopressor drug.
J.G.	53	150/92	102	0.5	80/50	5	72	Reversed by Neosynephrin

tive of weight and age. Nevertheless, the time, extent, and duration of decreases in blood pressure were similar. The vasodepression occurred rapidly and was usually maximal within 8 to 15 minutes. The range of decrease from the pressure prevailing before the drug was given varied between 18 and 156 mm. of mercury systolic, and between 10 and 110 mm. diastolic. The experiments were terminated in two to three hours, by which time the blood pressure had usually risen to above normotensive but was still below the premedication levels. In 3 patients the blood pressure decreased profoundly after one injection, and in a fourth patient (J.G.) after the second dose. As shown in Table 1, this occurred in 5 to 14 minutes and was most striking in patient E.G. No clinical manifestations of peripheral vascular shock were noted in these 4 patients, who remained alert and calm. Atropine and vasopressor drugs were given, as explained later, to arrest further vasodepression.

Chart 3 illustrates a pronounced response to two doses of Veratrone and then reversal of vasodepression by vasopressor drugs. Following the first injection of 0.5 mg. of Veratrone, the pressure dropped from 150 mm. systolic and 92 mm. diastolic to 106 mm. and 64 mm., and it increased only slightly during the following 45 minutes. Then another similar dose reduced the blood pressure to 80 mm. systolic and 50 mm. diastolic 5 minutes after injection. Neosynephrin® given intravenously promptly elevated the blood pressure to 194 mm. and 120 mm. but did not sustain it. Inasmuch as only 4 of the 22 patients had so pronounced a hypotensive effect, it is reasonable to assume that enhanced sensitivity or cumulative effect had occurred. This suggests the need for careful observation of the blood pressure in all patients for at least 30 minutes following injection of Veratrone.

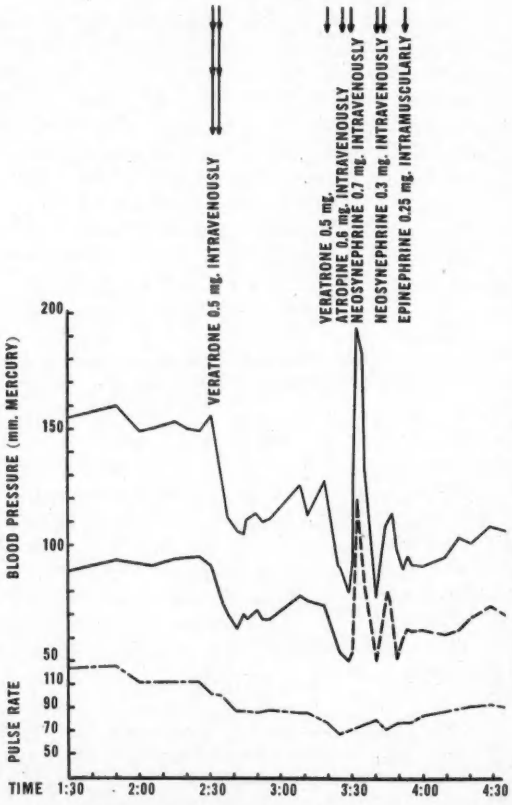

Chart 3.—Pronounced decrease in blood pressure in a patient (J.G.) following 0.5 mg. of Veratrone, and subsequent response to vasopressor drugs. See discussion in text and Table 1.

2. *Effect on the Heart Rate*

The effects on the heart rate are shown in Charts 1, 3, and 4. In all patients there was a decrease in heart rate ranging from 7 to 36 beats per minute. When atropine was administered during the hypotensive phase, the heart rate did not increase significantly.

3. *The Effect of Varying Doses and Intervals Between Injections*

The results indicate that a dose of 0.3 to 0.5 mg. of Veratrone will produce a satisfactory vasodepression in the average patient with essential hypertension and will also cause vasodepression in normotensive persons. The data also demonstrate that both dosage and rapidity of administration have pronounced effect on the hypotensive response. Thus, 0.8 mg. given rapidly in one dose will cause a greater decrease in blood pressure than 1.49 mg. given

TABLE 2.—*Effect of multiple doses of veratrum on the blood pressure.*

Case	Age	Blood Pressure Before Injection (mm. Mercury) systolic/diastolic	—Doses in Milligrams— First	Second	Third	Lowest Blood Pressure After First Dose	Time Between First and Second Dose (Minutes)	Lowest Blood Pressure After Second Dose	Time Between Second and Third Dose (Minutes)	Lowest Blood Pressure After Third Dose
T.F.H.	30	166/116	0.5	0.5		128/88	28	110/74		
J.I.G.	53	152/92	0.5	0.5		106/64	48	80/50		
P.O.G.	39	160/105	0.5	0.3	0.5	134/88	23	134/88	25	134/88
A.L.	66	240/130	0.16	0.16	0.3	240/130	5	240/130	17	112/80
J.H.M.	40	190/120	0.5	0.16		150/102	70	142/100		
F.S.	45	198/140	0.3	0.1	0.3	168/118	30	160/120	18	146/98
L.S.	53	160/102	0.3	0.1	0.3	150/100	20	154/100	21	134/88
R.J.W.	34	150/104	0.5	0.3		134/94	25	125/86		

slowly in divided doses about a half hour apart. When two doses of 0.5 mg. are injected about a half hour apart, usually an additional decrease in blood pressure occurs (see Charts 3 and 4). The data for 8 patients receiving multiple injections is summarized in Table 2. Patient P.O.G. received 3 doses of veratrum (0.5 mg., 0.3 mg. and 0.5 mg.) 23 and 25 minutes apart; a satisfactory decrease in blood pressure occurred after the first dose, but the decrease was not accentuated by the subsequent injections. This was the only patient who did not have further decrease in blood pressure when a second injection was given within 30 minutes of the first.

When the initial dose was small, as in A.L., who received 2 injections of 0.16 mg. each within 5 minutes, there was no vasodepression. In the same patient, another injection of 0.3 mg. decreased the blood pressure to 112 mm. systolic and 80 mm. diastolic from a control level of 240 mm. and 130 mm. When the initial dose was large, smaller doses given later caused only slight additional decrease in blood pressure or none at all (see data on patients J.H.M., F.S. and L.S. in Table 2). In patient L.S. the first and third sub-average doses had a minimal hypotensive effect while the second dose had none. In the case of patient T.F.H. (Table 2, Chart 4) the same dose repeated after a few days resulted in the same, or slightly less, vasodepression. This agrees with observations of Meilman and Krayer.[16]

Although, as might be expected, the greatest decreases in blood pressure occurred in persons with the highest initial pressures, there was not always a parallelism. There was also no correlation between the hypotensive effect obtained and the age or weight of the patient or the duration of the hypertension. The factor most closely related to the decrease in blood pressure was the size of the dose injected, but this effect was influenced also by individual variation in sensitivity to the drug.

TABLE 3.—*Effect of atropine when given before and when given after veratrum injection*

Case	Blood Pressure (mm. of Mercury) Before Medication systolic/diastolic	After Veratrum Followed by Atropine systolic/diastolic	After Veratrum Preceded by Atropine systolic/diastolic	Dose of Atropine
H.B.	172/130	90/68	136/110	1.2 mg.
T.F.H.	184/120	100/60	136/98	1.2 mg.
H.L.S.	190/130	146/82	160/104	1.2 mg.
R.J.W.	146/100	124/84	192/140	0.6 mg.

4. *Effect of Atropine*

It has been established[16] that atropine decreases the vagal stimulating action of veratrum alkaloids, but this has not been sufficiently studied in man. To further examine the mechanism of action of veratrum, atropine (usually in doses of 1.3 mg.) was given intravenously to 2 patients before veratrum was given and to 7 patients after veratrum had been given and hypotension had taken place. The data on 4 patients are summarized in Table 3.

In patient H.L.S., 0.3 mg. of veratrum lowered the blood pressure to 146 mm. systolic and 82 mm. diastolic from 220 mm. and 150 mm. Three weeks later the same patient received two doses of atropine (1.3 mg. each) 20 minutes apart followed by 0.3

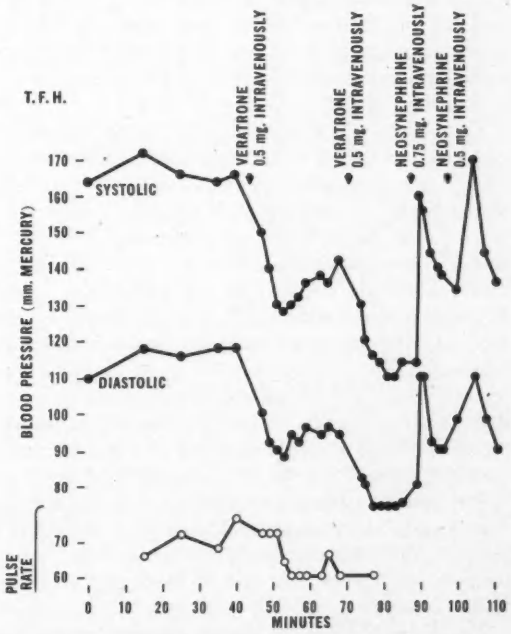

Chart 4.—Effect of two doses of 0.5 mg. (3 minims) of Veratrone and arrest of hypotension by Neosynephrin. Discussed in text.

mg. of veratrum and the blood pressure dropped from 190 mm. systolic and 130 mm. diastolic to 160 mm. and 104 mm. respectively.

When atropine was given during the hypotensive stage it usually arrested further vasodepression. In one patient (R.J.W.) who had blood pressure of 146 mm. of mercury systolic and 100 mm. diastolic and a pulse rate of 72, injection of veratrum in two doses, 0.5 mg. and 0.33 mg., caused a decrease in blood pressure to 124 mm. and 84 mm. and a slowing of the pulse rate to 48. Atropine, 0.6 mg., given intravenously 22 minutes after the last dose of veratrum, accelerated the pulse rate to 115 and elevated the blood pressure to 192 mm. and 140 mm. within eight minutes. This vasopressor response to atropine was exceptional. It probably was the clinical counterpart of the effect of veratrum alkaloids observed in animals, which is considered to be a manifestation of epinephrine release.[14]

These results show that atropine usually reduces but does not abolish the vasodepressor effects of veratrum.

5. *Effects of Vasoconstrictor Drugs*

The effects of vasoconstrictor drugs administered near the time of maximum decrease in blood pressure were studied. Neosynephrine given intravenously in doses of 0.3 to 0.7 mg. was usually employed, but occasionally epinephrine in doses of 0.25 mg. was given intramuscularly. In two experiments ephedrine sulfate (25 mg. intramuscularly and 2.5 mg. intravenously) was injected. All of these drugs reversed the vasodepression from veratrum, differences being only in rapidity and duration of their action.

The typical effects of giving Neosynephrin intravenously are shown in Charts 3 and 4. After veratrum had reduced the blood pressure to 114 mm. of mercury systolic and 75 mm. diastolic (Chart 4) from the average premedication level of 166 mm. and 116 mm., injection of 0.75 mg. of Neosynephrin caused the pressure to rise to 160 mm. and 110 mm. within 2 minutes. Then it decreased to 138 mm. and 90 mm. in 10 minutes. A second dose of 0.5 mg. of Neosynephrin caused a rise to 170 mm. and 110 mm. in 7 minutes. It is interesting to note that 13 minutes after the second dose of Neosynephrin the blood pressure was still at 136 mm. and 90 mm. In Chart 3 is shown comparable pressor response resulting from Neosynephrin, but of greater degree and shorter duration. The effects in these two patients illustrate that vasoconstrictor drugs only temporarily reverse the vasodepression resulting from veratrum.

These experiments demonstrated that veratrum, unlike other hypotensive drugs (hydrogenated ergot alkaloids,[11] for example) does not block the sympathetic vasoconstrictor reflexes. They also showed that vasopressor drugs do not abolish but only temporarily reverse the potent peripheral vasodilating action of veratrum, since the blood pressure returns to relative hypotensive levels after the pressor action has subsided.

6. *Subjective and Objective Symptoms*

Despite the pronounced changes in the blood pressure and in the electrocardiographic tracings when veratrum was administered, severe or disturbing symptoms were rare. The symptoms usually noted were:

a. Tingling, coolness or numbness about the lips, face, tongue and trunk, occasionally extending to the extremities. These phenomena began 2 to 3 minutes after injection and usually before the decrease in blood pressure occurred.

b. A sensation of warmth, usually about the mouth, forehead and chest, but occasionally generalized, was also noted before the hypotension developed.

c. Perspiration, most pronounced on the forehead, was noted at times during the maximum effect of veratrum.

d. At least half of the patients had slight nausea. Two of them had vomiting and retching that was quickly controlled by giving atropine intravenously.

e. Hiccough occurred in one patient but lasted only a few minutes.

f. Mild sensation of substernal pressure was noted by one patient 27 minutes after veratrum was injected. It lasted about 5 minutes. At that time the blood pressure had dropped from 215 mm. of mercury systolic and 132 mm. diastolic to 114 mm. and 74 mm. respectively.

The foregoing manifestations (except for the last two) were roughly proportional to the dose, occurred a few minutes after injection and before the onset of substantial vasodepression, and usually lasted 5 to 15 minutes. These observations are in accord with those of Meilman and Krayer.[16]

DISCUSSION

In the present experiments Veratrone was found to be a potent vasodepressor. Although the degree of change was not the same in all cases, the blood pressure was considerably reduced in all of the patients, hypertensive and normotensive. Subnormal blood pressure (without evidence of shock) was produced in only four patients. This suggests that peripheral resistance had decreased, as was shown by Fries and co-workers.[9] Krayer and Acheson's[14] finding of peripheral neurogenic stimulation indicates that the changes brought about by the veratrum alkaloids probably are owing to peripheral vasodilation

rather than to a generalized toxic circulatory effect. The absence of toxic or irreversible peripheral vasodilation is apparent from the rapid response to vasopressor agents like Neosynephrin. In addition, this finding demonstrates that veratrum does not block sympathetic vasoconstrictor responses (see also Fries and co-workers[9]). The hypotensive action of this drug may be halted (or decreased) by giving atropine intravenously. This is kindred to an observation by Meilman and Krayer[16] that when atropine was given simultaneously with protoveratrine, the decrease in blood pressure was more gradual and of lesser degree than it was when protoveratrine was given alone. The countering action of atropine indicates that vagal stimulation plays a role in the reduction in blood pressure caused by the veratrum alkaloids. Since sympathetic vasoconstrictor reflexes are not blocked and the degree of vasodepression may be arrested in part by atropine, a margin of safety exists in the use of this drug as compared with other agents such as tetraethyl ammonium chloride or dibenamine.

Bradycardia is not essential for the hypotensive result and the two effects do not parallel each other; there may be pronounced hypotension with little slowing of pulse. This is in agreement with observations by Fries and co-workers[9] and by Meilman and Krayer.[16] The bradycardia brought about by veratrum persists even after atropine is given intravenously, which indicates that veratrum has extravagal action on the pulse rate. Veratrum given to digitalized patients further depresses the sino-auricular node and causes auriculoventricular block, as occurred in two of the patients in the present study. Hence, the drug should be given with caution to digitalized patients. Similarity in action between veratrum and digitalis alkaloids was suggested by Fries and co-workers[9] who reported that both caused increased cardiac output and decreased systolic and diastolic pulmonary blood pressure in patients with congestive heart failure. The present findings add further evidence.

The rapidity, degree and duration of the decrease in blood pressure brought about in hypertensive patients by intravenous administration of Veratrone suggest that the drug can be used therapeutically. The disease states most suitable for such therapy would be those in which severe hypertension is the primary cause of the symptoms and may jeopardize the patient's life. Such conditions are eclampsia,[2] acute pulmonary edema or congestive heart failure[9] and severe or protracted headache due to hypertension.[16] Meilman and Krayer[16] reported good response with protoveratrine in a case of severe unremitting headache. The recently reported observation that veratrum decreases the peripheral resistance in the cerebral blood vessels[6] suggests the possible use of this drug in hypertensive encephalopathic conditions. In recent studies of malignant hypertension it was noted that veratrum considerably reduced blood pressure in that condition.[8]

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REFERENCES

1. Amann, A., and Schaefer, H.: Uber Sensible Impulse in Herznerven, Pfluger's Arch. f. d. ges. Physiol., 246:757, 1943.

2. Assali, N. S., Kistner, R. W., and Garber, S. T.: The effect of veratrum viride on urine volume, blood pressure and pulse rate in normal and toxemic pregnancy, Am. J. Obst. and Gyn., 58:90, 1949.

3. Barrow, J. G., and Sikes, C. R.: The use of purified veratrum viride alkaloids in the treatment of essential hypertension, Am. Heart J., 41:742, 1951.

4. Bezold, A. von, and Hirt, L.: Uber die Physiologischen Wirkungen des Essigsauren Veratrums, Untersuch. Physiol. Lab., Wurzburg, 1:73, 1867.

5. Bryant, R. D., and Fleming, J. G.: Veratrum viride in the treatment of eclampsia—II, J.A.M.A., 115:1333, 1940.

6. Crumpton, C. W., Friedland, C. K., Kuo, P. T., Schnabel, T. G., Foltz, E. L., Page, R. G., Alanis, J., and Kafkenschiel, J. H.: The hemodynamic effects of protoveratrine in essential hypertension, J. Clin. Inves., 30:634, 1951.

7. Dawes, G. S.: Studies on veratrum alkaloids—VII. Receptor areas in the coronary arteries and elsewhere as revealed by the use of veratridine, J. Pharmacol. and Exper. Therap., 89:325, 1947.

8. Elek, S. R., McNair, J. D., and Griffith, G. C.: The electrocardiographic effects of intravenous veratrum viride, Circulation, 7:903, 1953.

9. Freis, E. D., Stanton, J. R., Culbertson, J. W., Litter, J., Halperin, M. H., Burnett, C. H., and Wilkins, R. W.: The hemodynamic effects of hypotensive drugs in man—I. Veratrum viride, J. Clin. Inves.., 28:353, 1949.

10. Freis, E. D., and Stanton, J. R.: A clinical evaluation of veratrum viride in the treatment of essential hypertension, Am. Heart J., 36:723, 1948.

11. Freis, E. D., Stanton, J. R., Litter, J., Culbertson, J. W., Halperin, M. H., Moister, F. C., and Wilkins, R. W.: The hemodynamic effects of hypotensive drugs in man—II. Dihydroergocornine, J. Clin. Invest. 28:1387, 1949.

12. Jarisch, A., and Richter, H.: Die Afferenten Bahnen des Veratrineffektes in den Herznerven, Arch. F. Exper. Path. u. Pharmakol., 193:355, 1939.

13. Jarisch, A., and Zotterman, Y.: Depressor reflexes from the heart, Acta. Physiol. Scandinav., 16:31, 1948.

14. Krayer, O., and Acheson, G. H.: The pharmacology of the veratrum alkaloids, Physiol. Rev., 26:383, 1946.

15. McNair, J. D., Griffith, G. C., and Elek, S. R.: A prolonged study of oral veratrum viride in the treatment of essential hypertension, Am. Heart J., 40:382, 1950.

16. Meilman, E., and Krayer, O.: Clinical studies on veratrum alkaloids: The action of protoveratrine and veratridine in hypertension, Circulation, 1:204, 1950.

17. Richter, H., and Amann, A.: Ist die Lunge Chemosensible? Arch. f. Exper. Path. u. Pharmakol., 196:274, 1940.

A Cardiovascular Disease Case Progress Index

A Means of Aiding Research and Supplying Teaching Material

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• The establishment of a Cardiovascular Case Progress Index at the University of California School of Medicine is reported. The need for such an index to increase our knowledge of chronic cardiovascular diseases is discussed. Cases of various disorders of the cardiovascular system seen in a routine way in the hospital or outpatient department are listed in the Index, and their progress followed indefinitely. The organization, operation, and utilization of the Index for teaching and research are briefly discussed.

THE PRESSING NEED for more accurate information on the course and prognosis of chronic disease, particularly as they are affected by the newer medical and surgical therapy, is evident to all who are familiar with the subject. Since the turn of the century the life expectancy of persons in this country has been greatly increased. It is significant that many of the major causes of death and morbidity are now chronic diseases. Clearly, in the years ahead teaching and research in the field of medicine will increasingly emphasize these chronic conditions, particularly those pertaining to the cardiovascular system.

There are few adequate long-range studies of cardiovascular diseases in man. Lack of precise knowledge of the course and progress of these disorders is embarrassing as modern medical and surgical techniques are applied in their treatment. Many good long-range laboratory studies have been made on animals, but it is never certain to what extent the findings apply to human beings unless they can be checked in man himself.

The Cardiovascular Case Progress Index established at the University of California School of Medicine in San Francisco in January 1953 is expected to provide a matrix within which such studies may be carried out in human beings. The Index consists of a list of cases of various disorders of the cardiovascular system observed routinely in the hospital or outpatient department of the school of medicine. It includes a procedure for following the progress of these patients. It is hoped that, in time, a significant number of cases will be made available for teaching and research.

ORGANIZATION OF THE INDEX

The Cardiovascular Case Progress Index was developed by physicians and surgeons on the faculty of the school of medicine. It was formally established under the auspices of an interdepartmental board whose members were interested in various aspects of cardiovascular disease. The board included a pediatrician, cardiovascular surgeon, neurosurgeon, a physician with special interest in the physiology of the circulation, and several cardiologists. From the administrative side, the associate dean of the school of medicine and a representative of the hospital administration were members.

A major problem of the early planning period pertained to diagnosis. At first members of the board believed that it would be possible to select a limited number of cardiovascular diagnoses for the Index, but it soon became evident that agreement on diagnoses to be included would require protracted discussion and careful evaluation. As a compromise, certain categories of disorders of the cardiovascular system were selected. These are listed in the first column of the Registration Sheet (see sample, next page). It was agreed that cases in which the diagnosis fell into one or more of these general categories would be included in the Index. In each case the specific diagnosis is made in the usual manner according to *Standard Nomenclature of Diseases and Operations*, fourth edition, and entered in the appropriate space on the Registration Sheet.

It was recognized that certain associated disorders, diagnostic procedures, and therapeutic procedures as they pertain to each diagnosis might be important in determining groups from which generalizations could later be drawn. Accordingly, members of the board selected the specific items which appear in the second, third, and fourth columns of the Registration Sheet.

From the Cardiovascular Board, the Cancer Research Institute, and the Department of Medicine, University of California School of Medicine, San Francisco.

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REGISTRATION SHEET

Clinic or ward.....Hospital service.....

Name of physician registering case.....Date of reg.....

Initial diagnosis (4th ed., Standard Nomenclature).....

.....Std. Nom. No.....

.....

.....

Name of patient.....Unit No.....Sex: M.....F.....

Date of initial diagnosis*.....Age at initial diagnosis.....Race: W.....N.....Other.....

Check frequency of follow-up recommended: 3 months..... 6 months..... annual.....

Check as many of the listed conditions of the cardiovascular system, associated disorders, diagnostic procedures, and therapeutic procedures as apply to this patient.

check	code	Conditions of cardiovascular system
☐	1	Aneurysm
☐	2	Arrhythmia
☐	3	Arteriovenus communication
☐	4	Collagen
☐	5	Congenital
☐	6	Coronary
☐	7	Embolism
☐	8	Hemorrhage
☐	9	Hypertension
☐	10	Neurocirculatory asthenia
☐	11	Occlusion, artery
☐	12	Occlusion, vein
☐	13	Pericardium
☐	14	Pulmonary
☐	15	Renal
☐	16	Rheumatic
☐	17	Subacute bacterial endocarditis
☐	18	Syphilitic
☐	19	Thyroid
☐	20	Vasomotor
☐	21	Unusual pain syndrome
☐	30	Conditions, cause unknown
☐	40	Operation, specify

check	code	Associated disorders
☐	1	Anemia (less than 10 gms. hemoglobin)
☐	2	Atrophy, necrosis or gangrene
		Cardiac functional capacity
☐	3.1	Class I
☐	3.2	Class II
☐	3.3	Class III
☐	3.4	Class IV
☐	4	Cardiac hypertrophy
☐	5	Convulsions
		Coronary insufficiency
☐	6.1	Grade I (angina)
☐	6.2	Grade II (prolonged pain without infarction)
☐	6.3	Grade III (myocardial infarction)
☐	7	Diabetes mellitus
☐	8	Disorders of consciousness
☐	9	Edema
☐	10	Electrolyte disturbance
☐	11	Eye ground changes (KW3 only)
☐	12	Gout
☐	13	Papilledema (include KW4)
☐	14	Polycythemia
☐	15	P.O. bleeding
☐	16	Pregnancy
☐	17	Pregnancy, toxemia of
☐	18	Pulmonary embolism and/or infarction
☐	19	Pyelonephritis
☐	20	Renal insufficiency
☐	21	Rest pain (extremity)

check	code	Diagnostic procedures
☐	1	Angiography
☐	2	Ballistocardiogram
☐	3	Blood volume
☐	4	Cardiac catheterization
☐	5	Cerebral blood flow
☐	6	Nerve block
☐	7	Oxygen saturation
☐	8	Pheochromocytoma
☐	9	Phonocardiogram
☐	10	Pressure pulse recordings
☐	11	Psychiatric evaluation
☐	12	Pulmonary function test
☐	13	Pylogram
☐	14	Radioisotope studies
☐	15	Renal clearance
☐	16	Vasodilatation tests
☐	17	Vectorgram

check	code	Therapeutic procedures
☐	1	Blood and blood substitutes
		Drugs or medications
☐	10	Anticoagulant
☐	11	Autonomic blocking
☐	12	Procaine amide
☐	13	Quinidine
☐	14	Resin
☐	15	Vaso-constrictor
		Operations
☐	20	Heart
☐	21	Homologous graft
☐	22	Great vessels
☐	23	Sympathectomy
☐	24	Sympathetic anesthetization
☐	25	Vessel ligation, intracranial
☐	26	Vessel ligation, extracranial
☐	30	Non-cardiac
		Regulation
☐	40	Lipid
☐	41	Potassium
☐	42	Protein
☐	43	Sodium
☐	44	Other electrolyte

* Record date of patient's first admission (whether teaching or private case) on which the diagnosis of cardiovascular disease was made.

Note: If this patient is included in a special study group (recognized by the cardiovascular board for purposes of this registration) please identify investigation by name:.....

OPERATION OF THE INDEX

The Registration Sheet is completed by the physician in charge of the patient in either the hospital or the outpatient department. The physician is thus responsible for the accuracy of the diagnosis and the other items checked.

All information recorded on the Registration Sheet is transferred by a secretary to a Patient Name Index Card. Much of the information is coded. The patient's name, participation in a social service project, occupation, date of birth, sex, race and address are recorded on the card, together with other identifying data. The diagnosis in terms of *Standard Nomenclature of Diseases and Operations* is posted. The items checked on the Registration Sheet under the headings "Conditions of the cardiovascular system," "Associated disorders," "Diagnostic procedures," and "Therapeutic procedures" are recorded. The Patient Name Index Card includes a summary of all the information on the Registration Sheet.

A separate index is made for each of the following listings: Cardiovascular conditions, Associated disorders, Diagnostic procedures and Therapeutic procedures. Each of these indexes is identical in form, and classification is facilitated by use of topographic and etiologic numbers associated with each item.

A system has been developed to follow the progress of each case until death of the patient from any cause. Patients who are under the care of members of the staff of the school of medicine are reexamined at intervals at the time of their visits to the hospital or to outpatient clinics. If a patient reverts to the care of a private physician, the wishes of that physician are respected regarding further follow-up through the Index. The private physician may choose whether the patient (1) may have follow-up examinations for the Index in the outpatient department, arranged through the physician's office, (2) may be contacted directly by the Index to arrange for follow-up examinations in the outpatient department, (3) is not to be contacted by the Index at all, the physician agreeing to supply the follow-up information himself, or (4) is not to be included in the Index.

UTILIZATION OF THE INDEX

It is anticipated that the Index will have many uses for teaching and clinical research. Through its use, suitable patients for clinical demonstration to students and presentation at seminars may be easily located. Patients in various stages of a given disease or with various complicating conditions can be easily gathered for teaching purposes. In time the course of many chronic cardiovascular disorders, as evidenced by patients followed through the Index, will form the basis for more accurate teaching in this field. The effectiveness of diagnostic and therapeutic procedures can be evaluated for teaching and research.

It is expected that the Index will serve as a matrix for many clinical studies of a research character. It provides an ever-increasing number of carefully followed patients with various disorders of the cardiovascular system and a mechanism for identifying suitable patients for any particular study. Special or detailed studies may be carried out by reference to the patient's hospital and outpatient department record or by examination of the patient himself if this is necessary or desirable.

Finally, a study of the Index itself will yield useful information concerning the completeness and accuracy of diagnosis and registration. Data will be developed and analyzed to describe the population with various cardiovascular disorders included in the Index with reference to such characteristics as age, sex, and occupation. The frequency of diagnostic and therapeutic procedures and the incidence of associated non-cardiovascular disorders may be easily determined for any diagnosis. Special studies relating to hypertensive cardiovascular disease, arteriosclerotic heart disease and incompletely diagnosed conditions are currently being planned.

909 Hyde Street.

The General Practitioner in Industrial Medicine

ORRIS R. MYERS, M.D., Eureka

• *Most industrial injuries are treated by physicians who have a general practice in addition to their industrial work. Because of the increasing number and seriousness of industrial injuries, better preparation for treatment is required in the patient's interest and for reasonable economy. The trend toward centralization of industrial medical facilities, increasing before and during World War II, has been somewhat reversed; the general practitioner now has an opportunity to take a useful place in the care of injured employees.*

A physician dealing with industrial cases must be prepared to give immediate emergency treatment, to comply with the procedures of insurance carriers, and to refer cases which he is not skilled or equipped to handle. As a personal physician having the confidence of the patient he can secure greater cooperation from all parties concerned in industrial disability and can sometimes promote a more rapid recovery.

OF THE MORE THAN 500,000 industrial injuries reported by California physicians each year, over 60 per cent are treated by general practitioners. This latter designation includes a large number of physicians and surgeons with a general practice which is more than 50 per cent industrial.

At the time California's present workmen's compensation law was passed, the "family physician" or general practitioner treated practically all injuries, occasionally referring a case of major trauma. Today it is safe to say that most major injuries are treated by specialists or in consultation with them. This change has been brought about by the evolution of medical practice and also by certain developments in industry:

1. Increased amount of industry, with a greater number of accidents.

2. Expansion of those industries which have a higher rate of accidents.

3. Increased mechanization and speed, causing greater severity of accidents despite safety programs.

4. Increased motorization in industry and faster transportation, resulting in a greater number of vehicular accidents.

More definite treatment, demanding special skill and training, was required for the more severe and numerous injuries resulting from these conditions. Facilities beyond those available to the general practitioner are usually mandatory in major injuries.

Industrial insurors were quick to recognize this need as it became necessary for them to set up panels of physicians who they knew were qualified and equipped for industrial practice. In turn, physicians acquiring large industrial practices set up clinics, groups and other organizations which operated economically for the insurors and therefore for employers also. Many general practitioners, however, instead of qualifying themselves and making satisfactory arrangements for such practice, merely disapproved or condemned these developments. At the beginning of World War II, therefore, most industrial practice was being done by industrial groups, plant medical staffs, and even in industrial hospitals, and the medical and surgical service provided was usually good. In some instances the war enhanced these conditions; but after the war, possibly because of the opposition of organized medicine to socialization, there was a greater decentralization of industrial practice.

Nevertheless the average general practitioner, especially if he had had military service, learned from wartime conditions the value of integration, locally and regionally, of the medical profession including all specialties. With the organization of the Academy of General Practice there has developed a real effort at an equitable, honest and realistic solution to the problem of privileges and recognition of general practitioners.

Too many general practitioners formerly—as perhaps a few still do—looked upon insurance cases as an easy and inconspicuous means of enhancing their finances by padding accounts, ordering useless or unnecessary prolonged diathermy and heat treatments without supervision and billing these as physical therapy, and treating conditions for which they lacked experience and training, rather than following the concept, "as a conscientious disciple of Hippocrates, earning a reasonable living, with a security for old age and not expecting or trying to become a wealthy man through the practice of medicine." Too

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often they permitted themselves to become indolent, making no attempt to keep up with medical developments, especially in treating trauma, forgetting much and acquiring nothing to replace it. As more and better trained specialists became available—particularly in the fields of orthopedics and traumatology—employers, insurance carriers, and employees preferred and demanded this specialized service.

With the ever increasing number of accidents, both civilian and occupational, it behooved insurance companies and employers to pay heed to the type of medical service available and rendered. The cost for treatment of all accidents in 1951 was $7,900,000,000 and for that of occupational or industrial accidents was $2,650,000,000.

Can scientific treatment be compatible with compassion? It has been stated that physicians today know more about medicine than they do about patients. The author believes that in this regard the general practitioner has a place in medical and industrial integration, whether it be local, regional, or governmental, including the application of health insurance. He can well be the herald and exponent of good medicine and, at the same time, may be especially useful in psychologically evaluating the patient as a person.

The general practitioner can have a special position in the community of industry because of his intimate knowledge of the home environment and living conditions of the worker. In recent years employers in both large and small plants have taken an increasing interest in the health problems of their employees which extends to their homes. Claim examiners have long known the relation of home conditions to frequency and severity of injury. As was indicated in the discussions of the Annual Congress on Industrial Health, 1953, industrial medical and health organizations are much concerned as to the ability of the general practitioner to extend the scope of his service to the health problems of industry.

In order to render such services, however, a physician must have an office prepared for immediate emergency treatment and must make personnel in his office familiar with the forms and procedures of insurance practice. He must acquaint himself with the problems of his industrial community. He must be able to provide good modern treatment of trauma, either by his own skill and training or by definite arrangements with specialists who he knows can handle the more difficult problems for which the general practitioner is not trained. He must recognize his own limitations in accordance with the Principles of Medical Ethics, bearing in mind the objective of getting injured workers back to the job in the shortest time and with the best physical recovery.

It is not uncommon that an injured employee is seen by more consultants than are needed. They may or may not agree as to the degree of his disability, the nature of the injury and the treatment to be given, but the employee may feel that the insuror or employer is trying to find an excuse to conclude treatment or get him to work before he has fully recovered. Here the general practitioner, especially if he is the employee's personal physician, can be of great value in advising him, and often the period of disability is considerably reduced because of this personal relationship. Here is an opportunity for a real personal physician, or, to use the term of the Alameda-Contra Costa Medical Association, the patient's medical manager.

The personal physician need not fear to lose income by proper and necessary referrals. The specialist should likewise respect the Principles of Medical Ethics by seeing that the patient is returned to the care of the referring physician after the required special service has been rendered, and the insurance carriers also must respect this principle.

It may appear that this procedure involves dual service and cost, but in reality there is no additional expense. The general practitioner is simply receiving his share and recognition of the service rendered. In these times when medicine is striving for better public relations, such an arrangement will further that purpose.

The controversial problem of fee-splitting is pertinent to this discussion. There is a movement in Iowa and in Illinois to revise medical ethics in those states to permit a division of fees between the referring physician and the specialist, and there has been some indication of a similar tendency in New York and in California. This action is here mentioned only to be condemned; such a radical change is not necessary for an equitable fee, or to compensate both the referring physician and the specialist. The American Medical Association and the American College of Surgeons have long condemned fee-splitting.

The general practitioner has a very definite place in the field of industrial medicine and surgery. He cannot expect to participate without adequate training and proper facilities, and he should make known by precept and practice his willingness to call consultation whenever it seems in the best interest of the patient.

525 West Seventh Street.

The Cardiovascular System in Acute Infectious Disease

IRVING FINE, M.D., Walnut Creek

• *Myocarditis may result from a wide variety of acute infectious diseases, but electrocardiographic abnormalities interpreted as indicating myocarditis may arise from a number of other causes.*

Among the factors which may cause myocarditis are direct invasion by an organism, the toxic products of an organism, hypersensitivity to the products of an organism, drugs used in therapy, deficiency in nutrients, electrolyte imbalance, and, rarely, fever.

Recently emphasis has been placed on the finding that circulatory failure in acute infectious diseases is often primarily peripheral, although heart failure due to myocarditis is not uncommon.

THE TERM "MYOCARDITIS" has been loosely used to denote functional derangement of the myocardium during the course of infectious disease. A number of investigators have made clinical, electrocardiographic and autopsy studies of the heart in a variety of infectious diseases and a high incidence of concomitant "myocarditis" has been reported.[7, 16, 22, 31, 44, 45, 54, 55] The literature contains reports of cardiac abnormalities occurring with diphtheria,[4, 25, 35] scarlet fever and other streptococcal infections,[35, 36, 39, 41] infectious hepatitis,[11] bacterial pneumonia,[10, 24, 46, 63] typhoid fever,[6, 37, 38] gonococcal[53] and meningococcic infections,[30, 47] tuberculosis,[1, 66] typhus,[69] scrub typhus,[29, 50, 58] measles,[9, 21, 43] influenza A infections,[17] mumps,[42, 68] primary atypical pneumonia,[32] infectious mononucleosis,[14] poliomyelitis,[12, 20, 33, 48] and other infectious diseases.

Saphir[44] found evidence of myocarditis in 490 of 5,626 patients that died of a wide variety of infectious disease. Clinical studies have generally indicated a higher percentage of cardiac abnormality. In electrocardiographic studies Burnett and Piltz[7] noted abnormalities in 20 of 55 adults and in 8 of 45 children. Neubauer[31] studied 200 patients with infectious disease and made a diagnosis of myocarditis on clinical observation alone in 55 per cent and on electrocardiographic evidence alone in 24 per cent. Fine, Brainerd, and Sokolow[16] studied 84 patients with a variety of infectious diseases and found clinical and electrocardiographic evidence of myocarditis in about one-third. It is probable that the discrepancy between pathologic and clinical-electrocardiographic evidence of myocarditis arises from the fact that many of the clinical-electrocardiographic abnormalities are due not to true myocarditis but to other pathologic and physiological factors which will be discussed later in this presentation.

Saphir[45] described the heart in myocarditis as characteristically enlarged, with a soft, grayish-yellow myocardium and a few yellowish streaks or minute areas of hemorrhage. Microscopically the process is often patchy, with considerable variation in intensity from one area to another. Muscle necrosis, interstitial edema, and leukocyte infiltration may occur singly or in combination. Saphir emphasized that many sections must be cut and examined before the diagnosis of myocarditis can be excluded. Gore and Saphir[22] reported that of 1,402 instances of myocarditis surveyed at the Army Institute of Pathology, over 90 per cent were non-rheumatic.

Clinical evidence is usually present in myocarditis. The following signs and symptoms justify suspicion: Poor quality of the heart sounds, especially of the mitral first heart sound; a drop in systolic blood pressure of 20 mm. or more; gallop rhythm; pulse rate out of proportion to the fever—either tachycardia or bradycardia; systolic murmur; cardiac enlargement; pallor; cyanosis; vomiting; listlessness; precordial pain; irregularities of rhythm. Saphir[45] stated that myocarditis should be suspected if a patient with an infectious disease suddenly becomes worse without apparent cause.

The electrocardiogram is generally very helpful, especially if unipolar limb and precordial leads are used. The first change is often a broad-topped T wave. This is usually followed in a day or two by diphasic and inverted T waves. The PR interval may become prolonged. More serious conduction defects are not likely to occur except in diphtheritic myocarditis; here they are of grave significance, almost invariably of a fatal condition. RS-T abnormalities are usually minor and not of significance.

Presented in part before the regional meeting of the American Heart Association, October 23, 1952, San Francisco, California.

The QT interval may be prolonged. The QRS complex is generally not abnormal.

There are a number of factors that affect cardiac function during infectious disease. In diphtheria the toxin is almost certainly the cause of myocardial damage. This is probably also true of acute streptococcal infections, typhoid fever, bacterial pneumonia and other infections characterized by toxemia. In other diseases the heart may be directly invaded by the infecting organism. In pyemia from various causes, and in acute meningococcemia, metastatic infection of the myocardium has been noted.[44, 47] In benign viral diseases such as mumps, influenza A and infectious mononucleosis it must be postulated that the myocardium is attacked directly by the virus. It has been demonstrated that the virus of encephalomyocarditis directly invades the myocardium.[51]

Hypersensitivity such as occurs in rheumatic fever is a possible cause of myocarditis. Wallgren[66] expressed belief that pericardial effusion in tuberculosis is often due to a tuberculo-allergic reaction. Polyarthritis in gonococcal infections is sometimes a hypersensitivity phenomenon, and myocarditis may be of similar origin in such diseases.

The possible effect of drugs used in therapy must be considered. It has been shown, both clinically and experimentally, that sulfa drugs can cause interstitial myocarditis. They may also cause inflammatory lesions in the peripheral blood vessels indistinguishable from periarteritis nodosa.[19, 56] Emetine when used in the treatment of amebiasis may be cardiotoxic.[27]

Nutritional factors may contribute to myocardial disease. Simonson, Henschel, and Keys[57] reported that electrocardiographic abnormalities developed in a majority of young men undergoing 24 weeks of semi-starvation. Porter and Bloom[37] were of the opinion that heart involvement is not as great a problem in the present-day treatment of typhoid fever because high calorie diets rather than starvation are now used.

Anemia, preexisting or occurring as a result of infectious disease, results in increased work for the heart and in myocardial anoxia. The electrocardiogram may show RS-T and T wave abnormality as a result of anemia.[13]

Thiamine and niacin deficiency may develop during acute infectious disease. Deficiency in either of these vitamins is deleterious to the myocardium and may be reflected in RS-T, T wave, and conduction abnormalities in the electrocardiogram.[15, 67] Rachmilewitz and Braun[38] in a study of typhoid fever found that electrocardiographic abnormalities reverted to normal much faster in a group of patients given 300 to 600 mg. of niacin daily than in a control group.

Electrolyte imbalance frequently occurs during infectious disease. It has been shown that the acidosis and electrolyte imbalance occurring in diabetic coma often result in electrocardiographic abnormalities.[3] Alkalosis has been shown to cause a definite reduction in the amplitude of the T waves, while acidosis causes a striking increase in their height.[2] Hyperpotassemia results in high, peaked T waves, various degrees of heart block, and RS-T elevations.[61] Hypopotassemia results in low or inverted T waves, depression of RS-T, and prolongation of the QT intervals.[40, 60] The characteristic lesions in the heart in experimentally produced potassium deficiency consisted of myocardial and endocardial necrosis with replacement by scar tissue and infiltration by phagocytes.[18]

Reduction of ionized calcium in the serum results in typical changes in the electrocardiogram—prolongation of the QT interval, sharply pointed positive T waves and a long isoelectric course of ST. Dehydration can cause flattening of the T waves and depression of the RS-T segments.[5]

Fever has been thought by some investigators to be the cause of the electrocardiographic abnormalities seen in infectious disease. There have been a number of studies on the effect of fever on the electrocardiogram[8, 16, 26, 28, 52, 64] Most of these studies are in agreement that in only an occasional patient does fever per se cause electrocardiographic abnormality. The tachycardia associated with fever may cause a generalized lowering of the PQRST complex. A patient with poor coronary circulation may have clinical and electrocardiographic evidence of myocardial anoxia owing to the increased work load of the heart. The myocarditis of acute infectious disease generally appears after the patient has been febrile several days, has no relation to the height of the fever, usually persists after the patient is afebrile, and may not appear until that time.

Except in diphtheria, only rarely is there evidence of congestive heart failure if the patient has had no previous cardiac abnormality. There is very little correlation between abnormalities of venous pressure or circulation time and clinical evidence of myocarditis.[16, 55] Saphir, however, concluded from autopsy findings that many deaths occurring during acute infection were directly due to myocarditis, that sudden death due to myocarditis is not uncommon and that clinical signs of heart failure are often present.[46]

Of late the importance of the peripheral circulation in acute infection has received attention. Perry[34] studied the peripheral circulation in lobar pneumonia in adults. He made observations on the color of the skin, on blood pressure, on response of the skin vessels to histamine, to stroking, to epineph-

rine, and to the back-pressure required to obliterate the blanching caused by epinephrine. He noted that the contractile power of the capillaries was impaired and that recovery of the vessels was slow. He concluded that the circulatory failure in pneumonia is really a failure at the periphery. Greene[23] made similar observations on children with pneumonia and concluded that treatment should be directed at the peripheral circulation rather than the heart. Stead and Eket[59] agreed that while many patients with infectious disease die of circulatory failure, the failure is primarily peripheral rather than central. Peripheral circulatory failure may impair the blood supply to the heart and cause ST and T wave abnormalities difficult to distinguish from those of myocarditis.

In the treatment of circulatory failure in acute infection, therefore, it must be borne in mind that the failure is almost always primarily peripheral, resulting in reduction in volume of circulating blood and inadequate venous return. The output of blood is lowered and the venous pressure is decreased. Digitalis is useless in such circumstances and may be harmful, as it will not slow the heart rate and may diminish an already decreased cardiac output. The judicious use of blood and perhaps epinephrine and adrenocortical hormones may be of value.

However, when true heart failure is present, the ordinary measures should be used. Saphir[49] pointed out that the myocarditis of acute infectious disease is generally a very patchy process. Digitalis may be expected to increase the efficiency of the normal heart muscle fibers until the affected ones have recovered. A special problem arises, however, in diphtheria. In patients that have died from diphtheritic myocarditis, generally most of the myocardium is quite necrotic. The clinical experience has been that digitalis is of little value in the treatment of myocardial failure due to diphtheria, but there is little to lose in a trial of digitalis, since severe diphtheritic myocarditis is almost invariably fatal.

Acute heart failure sometimes develops in babies with bronchiolitis. The babies are generally not in a toxic state but have pronounced respiratory distress because of obstruction of the terminal bronchioles. It has been the observation of many pediatricians that digitalis may be life-saving when cardiac dilation, extreme tachycardia, hepatomegaly and other signs of heart failure develop. It may be postulated that the acute emphysema secondary to terminal bronchiole obstruction causes reduction in the capacity of the pulmonary vascular bed, which results in pulmonary hypertension. In addition the anoxia present causes an increase in pulmonary artery pressure. Anoxia also increases the work and decreases the efficiency of the heart. These factors result in acute dilation of the right ventricle which may develop into cardiac decompensation. Rarely, pertussis may cause a similar problem of cor pulmonale.[62, 65]

1885 Oak Park Boulevard.

REFERENCES

1. Auerbach, O., and Guggenheim, A.: Tuberculosis of the myocardium, Quart. Bull. Sea View Hosp., 2:264, 1937.
2. Barker, P. S., Shrader, E. I., and Ronzoni, E.: The effects of alkalosis and acidosis upon the human electrocardiogram, Am. Heart J., 17:169, 1939.
3. Bellet, S., and Dyer, W. W.: The electrocardiogram during and after emergence from diabetic coma, Am. Heart J., 17:169, 1939.
4. Boyer, N. H., and Weinstein, L.: Diphtheritic myocarditis, N.E.J.M., 239:913, 1948.
5. Broch, O. J.: The electrocardiogram in derangements of the organism's water and electrolyte metabolism, Acta Med. Scandinav., 126:157, 1946.
6. Brow, D. R.: The heart in typhoid fever, Canad.M.A.J., 20:606, 1929.
7. Burnett, C. T., and Piltz, G. F.: The electrocardiogram in the acute infections, J.A.M.A., 93:1120, 1929.
8. Clagett, A. H.: The electrocardiographic changes following artificial hyperpyrexia, Am. J. Med. Sci., 208:81, 1944.
9. Degen, J. A., Jr.: Visceral pathology in measles, a clinico-pathologic study of 100 fatal cases, Am. J. Med. Sci., 194:104, 1937.
10. DeGraff, A. C., Travell, J. C., and Yager, J. A.: Electrocardiographic study of the heart in lobar pneumonia, J. Clin. Investigation, 10:633, 1931.
11. Dehn, H., Feil, H., and Kinderknecht, K. E.: Electrocardiographic changes in cases of infectious hepatitis, Am. Heart J., 31:183, 1946.
12. Dublin, W. B., and Larson, C. P.: Pathologic findings in poliomyelitis, Am. J. Clin. Path., 13:15, 1943.
13. Ellis, L. B., and Faulkner, J. M.: Heart in anaemia, N.E.J.M., 220:943, 1939.
14. Evans, W. F., and Graybiel, A.: Electrocardiographic evidence of complications in infectious mononucleosis, Am. J. Med. Sci., 211:220, 1946.
15. Feil, H.: A clinical study of the electrocardiogram and of phases of the cardiac systole in pellagra, Am. Heart J., 11:173, 1936.
16. Fine, I., Brainerd, H., and Sokolow, M.: Myocarditis in acute infectious diseases: A clinical and electrocardiographic study, Circulation, 2:859, 1950.
17. Finland, M., Parker, F., Jr., Barnes, M. W., and Joliffe, L. S.: Acute myocarditis in influenza A infections, Am. J. Med. Sci., 209:455, 1945.
18. Follis, R. H., Jr., Orent-Keiles, E., and McCollum, E. V.: The production of cardiac and renal lesions in rats by a diet extremely deficient in potassium, Am. J. Path., 18:29, 1942.
19. French, A. J., and Weller, C.: Interstitial myocarditis following the clinical and experimental use of sulfonamide drugs, Am. J. Path., 18:109, 1942.
20. Gefter, W. L., Leaman, W. G., Jr., Lucchesi, P. F., Mohler, L. E., and Dworin, M.: The heart in acute anterior poliomyelitis, Am. Heart J., 33:228, 1947.
21. Giustra, F. T., and Wilson, D. C.: Myocarditis following measles, Am. J. Dis. Chil., 79:487, 1950.
22. Gore, L., and Saphir, O.: Myocarditis: A classification of 1402 cases, Am. Heart J., 34:827, 1947.
23. Greene, D.: Role of the peripheral circulation in pneumonia in children, Am. J. Dis. Child., 53:947, 1937.
24. Hitzig, W. M., King, A., Bullowa, J., and Fishberg, A.: Circulation in lobar pneumonia, J. Clin. Inves., 15:452, 1936.

25. Hoyne, A., and Welford, N. T.: Diphtheritic myocarditis, J. Ped., 5:642, 1934.

26. Krusen, F. H.: Studies on cardiac activity of human subjects during artificial hyperpyrexia, Am. J. Physiol., 126:540, 1939.

27. Kent, L., and Kingsland, K. C.: Effects of emetine hydrochloride on the electrocardiogram in man, Am. Heart J., 39:576, 1950.

28. Knies, P. T.: The electrocardiogram in induced fever, Am. Heart J., 22:804, 1941.

29. Levine, H.: Cardiac changes of tsutsugamushi fever (scrub typhus): An investigation into their persistency, War Med., 7:76, 1945.

30. Lowe, C. U., and Diamond, L. K.: Myocarditis and pericarditis in meningococcic infection, Am. J. Dis. Child., 75:660, 1948.

31. Neubauer, C.: Myocarditis in acute infectious disease, Arch. Dis. Child., 19:178, 1944.

32. Painter, J. F., Hicks, A. M., and Hartman, S.: Clinical analysis of primary atypical pneumonia, Ann. Int. Med., 24:775, 1946.

33. Peale, A. R., and Lucchesi, P. F.: The cardiac muscle in poliomyelitis, Am. J. Dis. Child., 65:733, 1943.

34. Perry, C. B.: Peripheral circulation in acute lobar pneumonia, Quart. J. Med., 1934, p. 273.

35. Place, E. H.: Heart in diphtheria and scarlet fever, N.E.J.M., 207:864, 1932.

36. Place, E. H., Faulkner, J. M., and Ohler, W. R.: Effect of scarlet fever upon the heart, Am. J. Med. Sci., 189:352, 1935.

37. Porter, W. B., and Bloom, N.: The heart in typhoid fever, Am. Heart J., 10:793, 1935.

38. Rachmilewitz, M., and Braun, K.: Electrocardiographic changes in typhoid fever and their reversibility following niacin treatment, Am. Heart J., 36:284, 1948.

39. Rantz, L. A., Spink, W. W., and Boisnert, P. J.: Electrocardiographic abnormalities following hemolytic streptococcus sore throat, Arch. Int. Med., 77:66, 1946.

40. Riley, J. A.: Renal and cardiac lesions in potassium deficiency due to chronic diarrhea, Am. J. Med., 8:115, 1950.

41. Roelsen, E.: Electrocardiographic studies in scarlet fever, Acta Med. Scandinav., 106:26, 1941.

42. Rosenberg, D. H.: Electrocardiographic changes in epidemic parotitis, Proc. Soc. Exper. Biol. & Med., 58:91, 1945.

43. Ross, L. J.: The electrocardiogram in measles, Am. J. Dis. Child., 83:282, 1952.

44. Saphir, O.: Myocarditis, Arch. Path., 32:1000, 1941; *ibid.*, 33:88, 1942.

45. Saphir, O., Wile, S. A., and Reingold, J. M.: Myocarditis in children, Am. J. Dis. Child., 67:294, 1944.

46. Saphir, O.: Myocarditis in pneumonia, Ann. Int. Med., 28:963, 1948.

47. Saphir, O.: Meningococcic myocarditis, Am. J. Path., 12:677, 1936.

48. Saphir, O., and Wile, S. A.: Myocarditis in poliomyelitis, Am. J. Med. Sci., 203:781, 1942.

49. Saphir, O.: Myocarditis, Am. Practitioner, 2:552, 1948.

50. Sayen, J. J., Pond, H. S., Forrester, J. S., and Wood, F. C.: Scrub typhus in Assam and Burma, Medicine, 25:2, 1946.

51. Schmidt, E. C. H.: Virus myocarditis, Am. J. Path., 24:97, 1948.

52. Schwemlein, G. Y.: Effect of elevated body temperature on the cardiovascular system and the electrocardiogram, Arch. Phys. Med., 28:165, 1947.

53. Shapiro, E., Lipkis, M. S., Kahn, J., and Heid, J. B.: Electrocardiographic changes in acute gonococcic arthritis and myocarditis simulating acute rheumatic polyarthritis, Am. J. Med. Sci., 217:300, 1949.

54. Shookhoff, C., and Taran, L. M.: Electrocardiographic studies in infectious diseases, Am. Heart J., 6:541, 1931.

55. Sigler, L. H., Nash, P. L., Stein, S., and Epstein, S.: The correlation of clinical electrocardiography and circulation time findings in determining the cardiac status in infectious disease, J. Lab. & Clin. Med., 25:24, 1939.

56. Simon, M. A.: Pathological changes following the administration of sulfonamide drugs, Am. J. Med. Sci., 205:439, 1943.

57. Simonson, E., Henschel, A., and Keys, A.: The electrocardiogram of man in semi-starvation and subsequent rehabilitation, Am. Heart J., 35:584, 1948.

58. Sokolow, M., and Garland, L. H.: Cardiovascular disturbance in convalescent tsutsugamushi disease, U. S. Naval Bull., 45:1054, 1945.

59. Stead, E., and Eket, R.: Peripheral circulation in acute infectious diseases, Med. Clin. N. Amer., 1387, Sept. 1940.

60. Stewart, H. J., Smith, J. J., and Milhart, A. T.: The electrocardiogram and serum potassium changes in familial periodic paralysis, Am. J. Med. Sci., 199:789, 1940.

61. Tarail, R.: Electrocardiographic abnormality in a case of uremia manifesting hyperpotassemia, Am. Heart J., 35: 665, 1948.

62. Thompson, A. R.: Congestive failure in whooping cough, Brit. J. Child. Dis., 34:273, 1937.

63. Thomson, K. J., Rutstein, D. D., Tolmach, D. M., and Walker, W. H.: Electrocardiographic changes during and after pneumococcus pneumonia, Am. Heart J., 31:565, 1946.

64. Vesell, H., and Bierman, W.: The electrocardiogram in fever, Am. J. Med. Sci., 191:484, 1936.

65. Walker, S. H.: Cardiac complications of pertussis, J. Ped., 40:200, 1952.

66. Wallgren, A.: Tuberculous heart disease, Acta Med. Scandinav. Supp., 196:132, 1947.

67. Weiss, S., and Wilkins, R. S.: The nature of the cardiovascular disturbance in nutritional deficiency states (beriberi), Ann. Int. Med., 11:104, 1937.

68. Wendkos, M. H., and Noll, J., Jr.: Myocarditis caused by epidemic parotitis, Am. Ht. J., 27:414, 1944.

69. Woodward, T. E., and Bland, E. F.: Clinical observations in typhus fever with special reference to the cardiovascular system, J.A.M.A., 128:1145, 1945.

CASE REPORTS

- **Repair of Extensive Decubitus Ulcer of 31 Years' Duration**
- **Mucocele of the Appendix Complicated by Torsion and Gangrene**
- **Cholecystitis and Cholelithiasis in a Sixteen-Year-Old Boy**
- **Tuberculous Lymphadenitis, Allergic Vasculitis and Phlyctenulosis**

Repair of Extensive Decubitus Ulcer of 31 Years' Duration

A. ESTIN COMARR, M.D., Long Beach

SUCCESSFUL CLOSURE of a decubitus ulcer more extensive, more bizarre, with more involvement of the bone and of longer duration than any other observed by the author is here reported.

A soldier then aged 24 years underwent a bilateral hernia operation in a United States Army hospital in France in 1918. While recovering from the operation he had an attack of tonsillitis. During the following week he noticed pain in the region of the knees and hips. The legs were unsteady, with the muscles stiff and control impaired. During 1919 he had attacks of tonsillitis almost every six weeks, and in November 1920 his tonsils were removed.

When the patient married in 1920 he was potent. At that time he was active and generally able to take part in sports, but his friends told him his running had become poor. There developed what he described as a change in sensation, "as if cloth covered the area of the skin which was touched." Concurrent with this decrease in sensation was a further decrease in motor power. In the spring of 1921 symptoms increased rapidly and by June 1921 the patient was almost completely paralyzed in both lower extremities. In August 1921 laminectomy was done; the patient was told that there were "inflammation and adhesions" around the spinal cord.

In 1921 a decubitus ulcer developed over the right ischium. This persisted with exception of a period of almost five months in 1923 during which it remained healed. In 1924 the ulcer became progressively worse and by 1930 another ulcer developed in the left ischial area. The two ulcers were eventually connected by a breakdown in the perineal area in 1935. The patient was confined almost completely to a wheelchair. During these years his wife changed the dressings.

Before the laminectomy in 1921, the patient had progressively increasing difficulty in starting the urinary stream. From 1921 on, he discharged urine only by catheter, which he inserted himself. One day in January 1950, he noticed that the catheter did not reach the bladder but passed through and out the perineal ulcer. Every time this occurred he would turn on his abdomen and his wife would guide the catheter past the large perineal opening of the urethra into the bladder.

During these years a pronounced sensitivity to drugs, antibiotics, adhesive tape, and any sort of rubber developed. The slightest contact with rubber caused a large efflorescence of the skin.

From the Paraplegia Service of Veterans Administration Hospital, Long Beach, and the School of Medicine, University of California at Los Angeles.

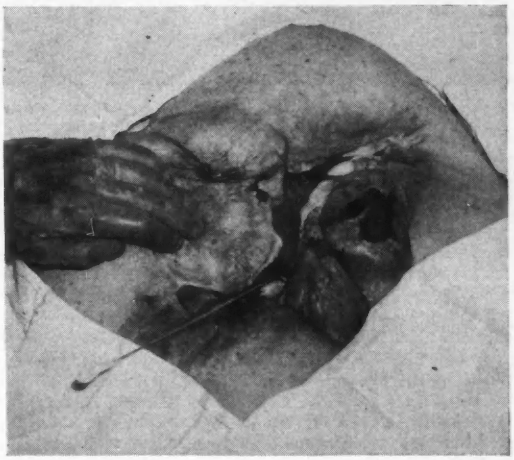

Figure 1.—The probe points to the bare catheter lying in the exposed urethra in the perineal portion of the decubitus ulcer.

On examination by a neurologist both lower extremities were observed to be atrophic and the feet were immobilized in a dropped position. There was no volitional motion in the lower extremities and the Beevor sign could not be elicited. The superficial abdominal reflexes could be elicited only faintly on the right and even more faintly on the left, above the umbilicus. The deep abdominal reflexes and the tendon reflexes of the knee and ankle joints were absent. Sensations of touch, pinprick, and vibration were absent below D4 bilaterally. The diagnosis was "chronic myelopathy, etiology unknown (possible arachnoiditis or transverse myelitis of infectious character), clinically complete at the segmental level of D4 with loss of function of both lower extremities and loss of sphincter control of bladder and bowel."

The ulcer extended about 12 inches from buttock to buttock, crossing the perineum; it averaged about 2 inches in width and was rather irregular. It was moderately undermined with necrosis at the base. The adjoining skin had superficial ulcerations. In the depth of the perineal portion of the ulcer, about one-half inch of the bare catheter was visible (Figure 1).

X-ray of the pelvis disclosed pronounced deformity of the right hip, apparently the result of an old fracture dislocation, surrounded by productive bony reaction. Both ischial tuberosities were absent, evidently because of erosion since the ulcer had never been operated upon. Some bone spicules were noted at the bone edges (Figure 2).

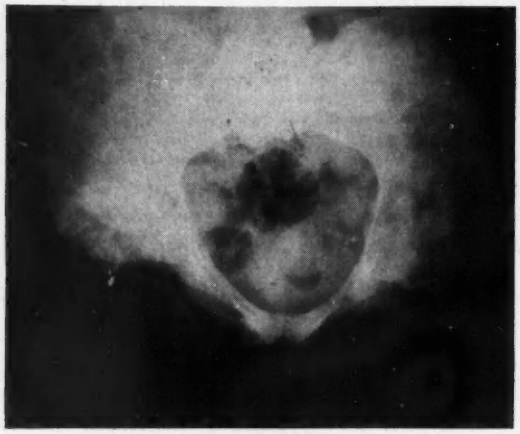

Figure 2.—Both ischial tuberosities are absent owing to erosion. Bone spicules are noted at the bone edges.

Daily immersion in brine was begun immediately in order to clean the ulcers.[2] Granulation tissue began to form.

On July 13, 1950, a permanent suprapubic catheter was introduced. The postoperative course was complicated by pronounced allergic dermatitis of the area surrounding the catheter which finally cleared when treated with dry heat and dry dressings. The perineal fistula healed after removal of the intraurethral catheter. Gradually the sensitivity disappeared, but operation on the ulcers was delayed because the patient's wife became acutely ill. In April 1952 the first stage of the closure was performed. All spicules of bone were removed from the ischial areas (Figure 3) with the surrounding pockets of granular and necrotic tissue. (Spontaneous amputation of the ischial bones had occurred.)

No attempt was made to achieve primary closure. Brine baths were continued until fresh granulation tissue appeared. After debridement the left ischial area was practically healed. On July 2, 1952, the second stage of the operation was performed to close primarily the perineal portion and the deep, undermined right ischial area. The entire lining was dissected out and the skin was widely undermined in all directions in order to form flaps. The perineal skin was mobilized as close to the rectum as was safely possible. Large masses of fat were excised from the perineal area and old scars in the gluteus muscle were resected superiorly in order to flatten the area. The skin was then easily closed with three button-retention sutures of wire. Two Penrose drains were inserted through puncture wounds at the base of the inferior skin flap. Two drains were brought out also at each wound angle and mattress-on-edge sutures of No. 32 stainless steel wire were used for closing the skin. Over a period of ten days the drains were gradually removed. The wound healed by primary intention except for a small area of necrosis which granulated quickly on treatment by baths and exposure to sun. The result was excellent (Figure 4).

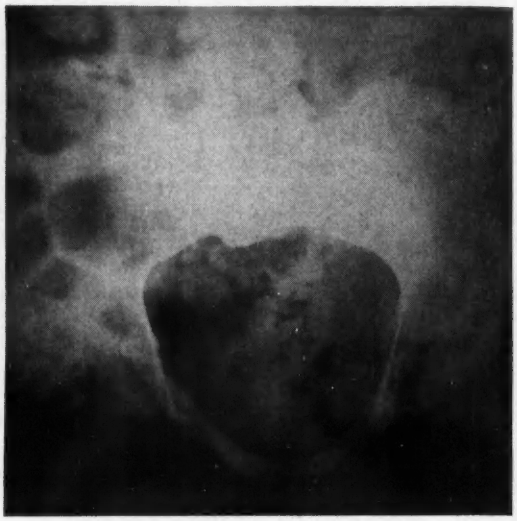

Figure 3.—The pelvis after spicules of bone were removed at the first stage of the operation.

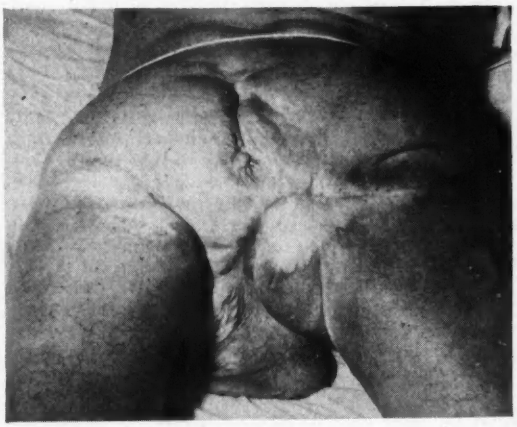

Figure 4.—The ulcer is healed for the first time in 31 years.

DISCUSSION

Several features are of interest in this case:

1. The duration of the decubitus ulcer, exceeding by far that of any other instance observed at this center in patients with spinal cord injuries incurred in World War I. Despite the long period over which the lesion remained open and despite the severity of the process manifested by complete erosion of the ischial bones, it is remarkable that amyloidosis did not occur, as it sometimes does much earlier in such cases.

2. The absence of malignant changes. On microscopic examination this ulcer was found to be benign. In another patient of the same age group with a sacral ulcer caused by a spinal cord injury during World War I, a cancer developed after a much shorter time but, after radical operation, did not recur in more than five years. Since that patient was the only one observed at the hospital in whom cancer developed from decubitus ulcer and since no similar case has been reported, it must be concluded that malignant degeneration of a decubitus ulcer is much rarer than progressive amyloidosis which, although not common, has been observed by the author and reported by others.[3]

3. The remarkable power of recuperation and the resulting operative cure. Obviously, without diversion of the urinary stream by suprapubic cystostomy any attempt at closure would have failed. The perineal fistula resulting from necrosis of a half-inch of the urethra, and the serious and prolonged imbalance of bladder control due to lesion of the

spinal cord, together with absence of skin, made any plastic repair with reconstruction of the urethra at this region impossible, in contrast to the management of urethral fistula located at the penoscrotal junction.[1] The health of the patient improved greatly, since the buttocks became covered with skin for the first time in 31 years; the uroseptic symptoms of chills and fever subsided completely as the suprapubic cystostomy began to function well. With continuing good care the patient has a good life expectancy.

SUMMARY

The case is reported of a 55-year-old veteran of World War I in whom a clinically complete cord lesion developed at the level of D4 after repeated bouts of tonsillitis. Decubitus ulcers occurred on both ischial regions, joined by extension to the perineum, and caused a perineal urethral fistula. After diversional suprapubic cystostomy, operative closure in two stages succeeded although the ulcer had persisted over a period of 31 years and despite extensive bone erosion which led to what amounted to spontaneous amputation of the ischial tuberosities.

REFERENCES

1. Comarr, A. E., and Bors, E.: Pathological changes in the urethra of paraplegic patients, J. Urol., 66:355-361, Sept. 1951.

2. Comarr, A. E.: Management of paraplegic decubitus ulcers, Ann. West. Med. & Surg., 3:235-240, July 1949.

3. Thompson, C. E., and Rice, M. L., Jr.: Secondary amyloidosis in spinal cord injury, Ann. Int. Med., 31:1057-1065, Dec. 1949.

Mucocele of the Appendix Complicated by Torsion and Gangrene

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MUCOCELE OF THE APPENDIX is an unusual condition and the complication of torsion and gangrene, as in the case herein, has been reported only twice previously.[6,7]

From a review of reports in the literature on large series it appears that mucocele is present in about 0.2 per cent of cases in which the appendix is removed; that the incidence is slightly greater in females than males; and that the condition occurs most often in the fourth, fifth and sixth decades of life, although instances have been reported between the ages of 4 and 70.

Results of studies of rabbits by Grodinsky and Rubnitz[5] and Cheng[4] indicated that the pathogenic sequence in the development of mucocele is: obliteration of the appendicial lumen in the absence of suppuration; active secretion of the mucosa; gradual distention of the appendix. In man, inflammation is the most definite and common factor causing mucocele. It is noteworthy that in many reported cases mention is made of a history suggestive of appendicitis which subsided spontaneously. Other reported causes of mucocele are carcinoid tumor of the appendix, appendicial abscess, and adenocarcinoma, endometrioma and tuberculosis of the cecum. The association of mucocele of the appendix and pseudomyxoma peritonei resulting from rupture of an ovarian cystadenoma has been frequently observed, but the relationship is not clear.[3] Rosenfeld[9] stated that mucocele of the appendix occurs in 25 per cent of such cases.

Mucoceles vary in size from slightly larger than a normal appendix to as much as 30 cm. in length. With gradual progressive distention the muscularis undergoes attenuation and fibrous tissue replacement. The wall in larger specimens in which mucocele has been present a long time may consist of only thin bands of hyalinized fibrous connective tissue with extensive areas devoid of mucosa. In the early stages the mucous content of a mucocele is clear and viscid; later it becomes gelatinous and turbid. The presence of small globular bodies of inspissated mucoid material in the dilated lumen has been referred to as "myxoglobulosis."

The most common complication of mucocele—rupture and the extrusion of the contents into the peritoneal cavity—may initiate pseudomyxoma peritonei. Rubnitz and Herman,[10] Cheng[4] and Bergan[1] have presented experimental evidence strongly supporting the postulation that pseudomyxoma peritonei of appendicial origin is a type of foreign body peritonitis resulting from mechanical or chemical irritation. Other complications include intussusception, acute inflammation and inclusion in hernial sacs. In one of several cases of calcified mucocele reported upon by Ostrum and Miller,[8] multiple fistulas developed following rupture of the tumor.

Often a mucocele is entirely asymptomatic and is noted only fortuitously in the course of abdominal or pelvic surgical procedures. When there are symptoms they are more often than not poorly defined—vague abdominal pain or tenderness in the right lower quadrant of the abdomen, sometimes associated with nausea or other manifestations of digestive disturbance. Acute symptoms occur with the various complications and depend on the complication. However, in several reported instances the first evidence of pseudomyxoma peritonei was the unexpected finding of mucinous material in a hernial sac during herniorrhaphy.[3] The difficulty in clinical diagnosis because of the lack of pathognomonic signs and symptoms is attested by the rarity of correct preoperative diagnoses. The only reported correct preoperative diagnoses have been accomplished by the demonstration of a mucocele during roentgen studies with barium enema.[2] Palpable mucoceles have been considered preoperatively as renal, retroperitoneal, cecal, uterine or ovarian masses. In the majority of reported cases in which symptoms were present the preoperative diagnosis was chronic appendicitis.

The treatment is surgical. If rupture has occurred just before operation or occurs during removal of the tumor, the patient can be expected to recover if all the extruded material is carefully removed. If there has been a large volume of mucocele content in the peritoneal cavity for a long time, the prognosis is grave.

REPORT OF A CASE

A 60-year-old Caucasian woman entered the hospital with chief complaint of pain in the lower abdomen, most severe in the right iliac area. At the onset, three days earlier, the pain had been generalized in the abdomen but in the previous 24 hours it had localized. The patient was nauseated and had vomited several times the first day. There was no antecedent history suggestive of appendicitis.

The patient was well developed and well nourished and did not appear to be acutely ill. The systolic blood pressure was 120 mm. of mercury and the diastolic pressure 78 mm. The pulse rate was 90. The temperature was 98.4° F. Tender to palpation throughout, the abdomen was exquisitely tender in the right iliac area and there was involuntary guarding over both lower abdominal quadrants. The uterus was small and mobile and the adnexa normal. Pain in the right adnexal area occurred upon manipulation of the

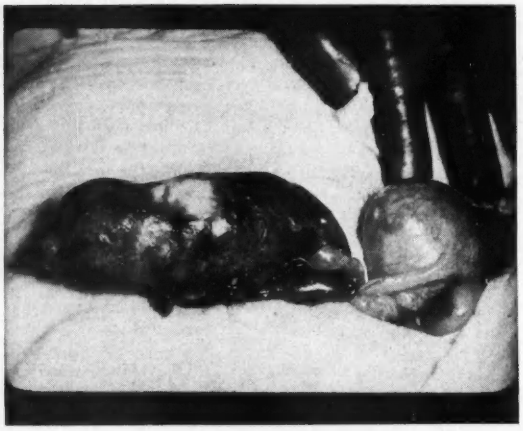

Figure 1.—Gangrenous mucocele of the appendix with the cecum delivered through the abdominal incision. Note the torsion of the undilated appendicial base.

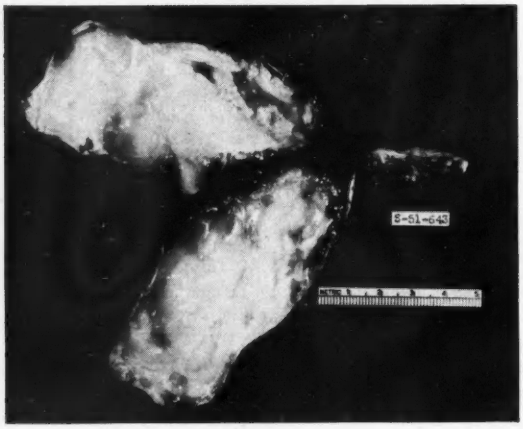

Figure 2.—Longitudinal section of the surgical specimen, showing the contents of the mucocele.

cervix. Leukocytes numbered 15,000 per cu. mm. of blood. Results of urinalysis were within normal limits. A diagnosis of acute appendicitis was made and operation was begun three hours after admittance to the hospital.

The peritoneal cavity, entered through a low paramedian abdominal incision, contained a moderate amount of serosanguineous fluid. A deeply cyanotic sausage-shaped tumefaction of the appendix was delivered into the operative field. The tumor had undergone torsion, consisting of two complete rotations, at the junction of the undilated proximal quarter of the appendix and the dilated distal three-quarters (Figure 1). Appendectomy was accomplished without difficulty. Convalescence was uneventful and the patient left the hospital on the eighth postoperative day.

Pathologist's report. The appendix, with a sausage-shaped tumefaction of the distal three-quarters, weighed 106 gm. The proximal undilated segment was 35 mm. long and 5 mm. in diameter and its lumen was obliterated in the distal 10 mm. Beyond the obliteration was a dilated tense mass 115 mm. long and 40 mm. in diameter. The serosa was smooth, glistening gray-purple, mottled with dark red. The mesoappendix was thickened and hemorrhagic. The leathery wall varied from 0.5 mm. to 2 mm. in thickness and contained spicules of calcification. The gelatinous content was translucent gray to opaque dull yellow (Figure 2). Upon microscopic examination of a section, the wall was observed to be composed of compact laminations of hyalinized collagen connective tissue infiltrated with occasional lymphocytes, plasma cells and neutrophilic polymorphonuclear leukocytes. There was no mucosa. Fine calcifications were imbedded along the inner surface. Compressed smooth muscle, present only on the mesoappendicial border, was undergoing necrobiosis. Dilated veins and dense extravasations of erythrocytes were noted throughout the wall, particularly in the less compact subserosa. In the undilated proximal segment the lumen was obliterated by dense fibrous connective tissue.

Pathologic diagnosis: Mucocele of the appendix with early gangrene.

SUMMARY

A case of mucocele of the appendix complicated by torsion and consequent gangrene is reported. Two previous instances of this complication have been recorded.

18 Canon Drive.

REFERENCES

1. Bergan, F.: Pseudomyxoma peritonei e processu vermiforme—an experimental study, Acta path. et microbiol. scandinav., 27:537, 1950.

2. Bonnan, L. J., and Davis, J. G.: Retroperitoneal mucocele of the appendix, Radiology, 51:375, 1948.

3. Bunch, G. H.: Mucoid disease of the appendix, Ann. Surg., 121:704, 1945.

4. Cheng, K. K.: An experimental study of mucocele of the appendix and pseudomyxoma peritonei, J. Path. and Bact., 61:217, 1949.

5. Grodinsky, M., and Rubnitz, A. S.: Mucocele of the appendix and pseudomyxoma peritonei, S. G. & O., 73:345, 1941.

6. Heatley, T. F.: Hemorrhagic mucocele of the appendix, J.A.M.A., 112:1935, 1939.

7. Lentino, A. S.: Appendicular mucocele and torsion of the appendix, Semana Med., 1:254, 1946.

8. Ostrum, H. W., and Miller, R. F.: Calcified mucocele of the appendix with rupture, Radiology, 36:356, 1941.

9. Rosenfeld, E. D.: Peritoneal pseudomyxoma, Arch. Path., 48:255, 1949.

10. Rubnitz, A. S., and Hermann, H. T.: Experimental appendicial mucocele, myxoglobulosis and peritoneal pseudomyxoma, Arch. Path., 36:297, 1943.

Cholecystitis and Cholelithiasis in a 16-Year-Old Boy

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THE AMERICAN MEDICAL LITERATURE contains little information on gallbladder disease in children and adolescents. Infants and children rarely have calculi in the gallbladder.[1] Acute cholecystitis, when it occurs in childhood, frequently is associated with bacterial infection such as scarlet fever, typhoid fever and septicemia.[1] Complications from obstruction of the gallbladder by intestinal nematodes have been reported.[1] Cholelithiasis in childhood is considered by some investigators to be in most cases a complication resulting from sickle cell anemia in Negroes and from congenital hemolytic anemia in Caucasians. Reports of cases in which coexistence of cholecystitis and cholelithiasis was proved by pathological examination, as in the following instance, are few.

REPORT OF A CASE

A 16-year-old Caucasian male had pain in the right upper quadrant of the abdomen that had increased in severity in the eight hours since onset. It was associated with nausea and vomiting. At first colicky, the pain had become more steady and penetrating and was referred to the lower ribs and back on the right side. In the preceding 13 years the patient had had attacks of pain in the same area, but less severe, at intervals of from one to six months. Usually they lasted a few minutes to a few hours. Physicians who had treated him from time to time were said to have ascribed the pain to "nervous spasm" of the stomach.

Upon examination it was noted that the pain was definitely localized in the right upper quadrant of the abdomen and there was some rebound tenderness. The oral temperature was 99 degrees F. Administration of 0.3 mg. of nitroglycerine brought about partial relief of pain but it was necessary to give 75.0 mg. of Demerol® for complete remission. In light of the severity of the pain the patient was hospitalized. When examination was carried out in the hospital, pain was elicited more readily in the right upper quadrant of the abdomen. Rebound tenderness was somewhat greater than before and there was tenderness over McBurney's area. Right rectus spasm and rigidity were noted, with tenderness greater on the right side of the rectus than the left. Nausea and vomiting persisted. The temperature was 98.4 degrees F. Demerol, 100 mg. every four hours, was required for relief of pain. In roentgen study of the upper gastrointestinal tract no evidence of intrinsic pathologic change in the stomach or in the duodenum was observed.

Erythrocytes numbered 4,850,000 per cu. mm. of blood and the hemoglobin content was 14.8 gm. per 100 cc. Leukocytes numbered 12,000 per cu. mm.—80 per cent segmented cells, 14 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. The icteric index was 7. Erythrocyte fragility was within normal limits. No abnormalities were noted in urinalysis.

As it could not be determined whether the patient had acute gallbladder disease or appendicitis with the appendix in a high retrocecal position, the abdomen was opened in a way to make both organs accessible. A right rectus incision was made down to the peritoneum, and when the peritoneum was opened much fluid was observed. The appendix, which was slightly inflamed but not enough to cause the symptoms, was amputated. When palpated, the gallbladder was noted to be firm, distended and adherent to the liver. The operative incision was extended two inches and the gallbladder was freed from the liver and removed.

Except for rapid pulse rate and spiking temperature for several days, recovery was uneventful.

PATHOLOGIST'S REPORT

Macroscopic. The appendix, 7.5 cm. long and 0.5 cm. in diameter, was moderately inflamed and there was soft fecal material in the lumen. The mucosa was smooth and pale. The gallbladder, 8x4.5x4.5 cm., had a constricting band part way around it about 2.5 cm. from the proximal end. The mucosa was mottled with patches of red, green and gray and there were reddened fibrous tags on the surface. The lumen was distended and contained very thick dark green bile, a large number of irregularly shaped small dark green calculi and considerable mucus. The wall, mottled like the mucosa, was thick and edematous. Upon examination of the sectioned surface an annular zone of thickening with tough and rather densely fibrous tissue was noted in the region of the constriction previously mentioned.

Microscopic. Much fat and fibrous tissue was observed in the submucosa of the appendix and there were large groups of lymphocytes throughout the wall and fairly numerous eosinophils in the muscularis and serosa. Hemorrhagic necrosis was noted in much of the mucosa of the gallbladder and in the adjoining muscular coat, with extensive infiltration of neutrophils, eosinophils, histiocytes, and lymphocytes. In a portion of the liver adherent to the gallbladder there was extensive interstitial infiltration of lymphocytes. Histiocytes and eosinophils were present in smaller number. There was much necrosis of liver cells, and bile pigment was noted in liver cells, phagocytes and bile capillaries.

Pathologic diagnosis: Healing (subacute) appendicitis; acute and chronic cholecystitis; cholelithiasis; subacute hepatitis with zone of parenchymatous degeneration.

SUMMARY

A case of cholecystitis with cholelithiasis in a 16-year-old Caucasian male is presented. Since it does occur in children, although rarely, it is important to consider gallbladder disease in differential diagnosis when dealing with acute disease of the abdomen in a patient in this age group.

3600th Medical Group, Luke Air Force Base, Phoenix, Arizona.

REFERENCE

1. Mitchell, Nelson: Textbook of Pediatrics, W. B. Saunders Company, Philadelphia, 4th edition, page 680, 1947.

Tuberculous Lymphadenitis, Allergic Vasculitis and Phlyctenulosis

Report of a Case

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VASCULITIS as a manifestation of hypersensitivity to the tubercle bacillus is well known. Erythema nodosum and erythema induratum are generally considered to be vascular hypersensitive reactions that are sometimes due to tuberculosis. Gilrane and Cherry[5] recently pointed out the histologic similarity of polyarteritis nodosa and erythema nodosum. Both are basically vasculitis and both are probably hypersensitive reactions, but erythema nodosum is known to be frequently a hypersensitive reaction to tuberculosis. In a given case, whether or not the allergic vasculitis is due to tuberculosis is important, for evidence is accumulating[2] that corticotropin (ACTH) and cortisone are sometimes harmful to patients with tuberculosis, whereas these hormones are effective in the treatment of periarteritis nodosa.

The clinical appearance of phlyctenular keratoconjunctivitis is characteristic and easily recognized. Phlyctenulosis is almost always an allergic manifestation of tuberculosis.[1,7]

Following is a report of a case considered one of periarteritis nodosa for 18 months because of the clinical and histologic manifestations, and in which corticotropin therapy was given, until the appearance of phlyctenules uncovered the etiologic agent of the allergic vasculitis.

REPORT OF A CASE

The patient, an 18-year-old boy, a native of Guam, first noted pain and swelling in the feet and ankles in March 1951. In June 1951, he was treated with sulfisoxazole at Tripler General Hospital for one month. In September 1951 he again noted gradual onset of pain in the ankles. This

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Presented before the Ophthalmology Section of the San Francisco Medical Society, November 4, 1952.

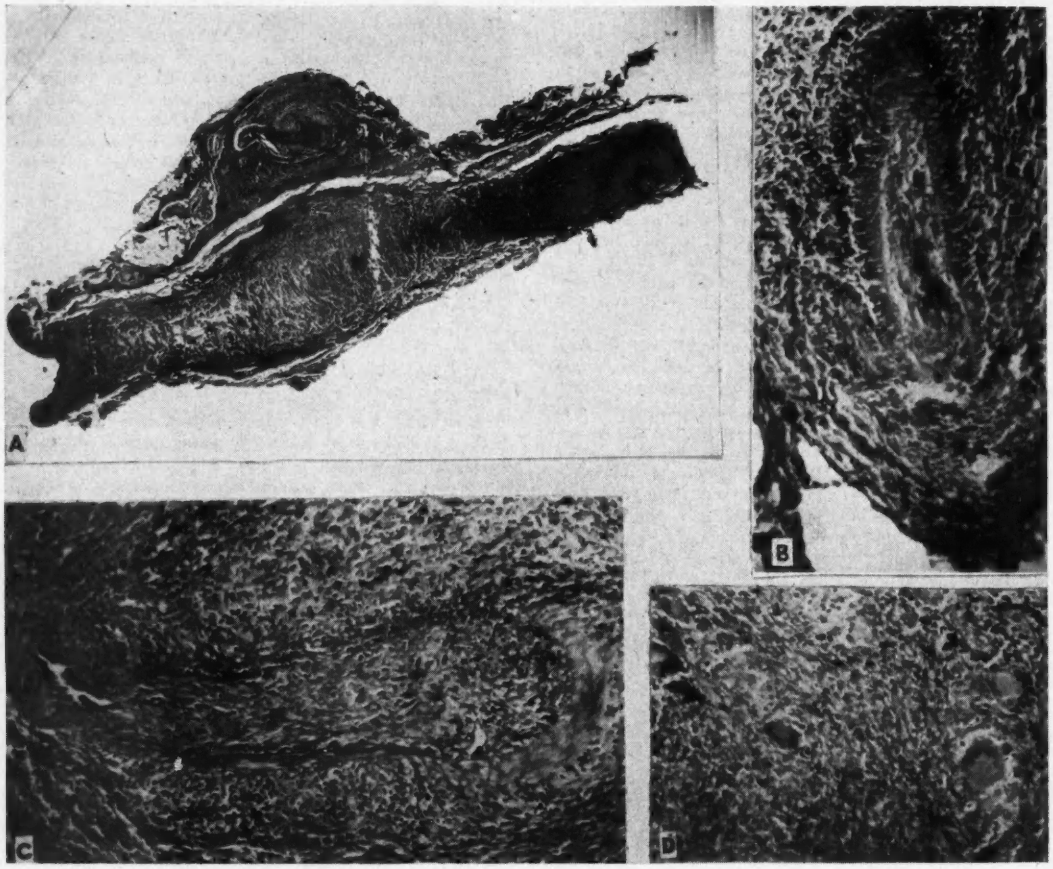

Figure 1.—Microscopic appearance of subcutaneous nodules. *A.* Inflamed artery and adjacent vein. *B.* Inflamed artery with broken elastic lamella. *C.* Inflamed and necrotic artery. Note inflammatory tissue in lumen. *D.* Section showing giant and epithelioid cells.

time tender nodules were present in the skin of the legs and the ulnar borders of both arms. From then on, nodules recurred in those areas many times. The patient complained of occasional dull substernal pain and dyspnea on exertion. Biopsy of a nodule of the right forearm at Tripler Hospital was highly suggestive of periarteritis nodosa. Corticotropin was given by vein intermittently over a two-month period and the condition improved. A specimen was taken from a nodule in the posterior aspect of the left calf, and again intimal proliferation of the wall of the artery with perivascular lymphocytic infiltration was observed.

The patient entered the Veterans Administration Hospital, San Francisco, March 25, 1952. No abnormalities were noted in x-ray films of the chest, in examinations of the urine and the blood, or in studies of the gastrointestinal tract and nervous system. One axillary lymph node, 1x2 cm., was felt.

On June 6, 1952, biopsy specimens were taken from the right forearm, wrist and leg. Moderate lymphocytic infiltration was noted upon examination of sections. There were thrombosed arteries, arterioles and veins with extensive necrosis of their walls. In one section features of a tuberculoid reaction were noted, with several giant cells (no bacilli were found). In another slide there was an excess of eosinophils. The specimens were obtained from Tripler Hospital, and upon comparison it was concluded that the condition was a pleomorphic one, and that while it could possibly be produced by erythema nodosum, Bazin's erythema induratum or migratory vasculitis, the degree of change in the vessels was most consistent with periarteritis nodosa (Figure 1).

After three weeks of relatively good health, fever recurred and the patient was readmitted to hospital July 28, 1952. He had had occasional bleeding from the nose for several days and some discharge of bright blood from the rectum after bowel movements, but had noted no blood in the urine, burning on urination, hemoptysis, cough or dyspnea. The patient complained of pain, redness and lacrimation of the right eye. A history of occasional increased formation of tears in the right eye over a period of many years was elicited. Vision was normal bilaterally. A pustular ezcematous area was noted about the left nostril. The right conjunctiva was moderately inflamed. There were three yellowish nodules about 2 mm. in diameter, having the appearance of recently formed phlyctenules, near the limbus of the right eye, and several similar nodules were noted on other parts of the conjunctiva (Figure 2). A number of scars of old phlyctenules were noted on the cornea and there was vascularization at the periphery of the cornea.

The axillary lymph nodes were 2 x 3 cm. in diameter. Cervical and inguinal nodes were palpable and small. Small nodules were noted on the posterior aspect of both calves and the lateral side of the left foot. No other abnormalities

Figure 2.—Three phlyctenules are in characteristic position at the limbus. Other phlyctenules are seen scattered on the conjunctiva.

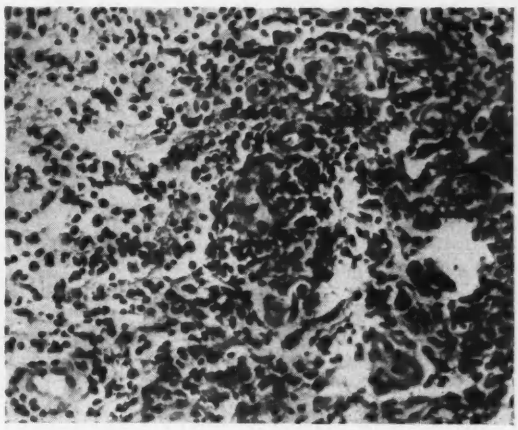

Figure 3.—Microscopic appearance of phlyctenule: a subepithelial accumulation of lymphocytes and macrophages.

were observed in physical, laboratory and roentgen examinations.

A diagnosis of phlyctenular keratoconjunctivitis was made and it was considered probable that the disease was due to hypersensitivity to the tubercle bacillus. Drops of cortisone were instilled in the right eye every hour during the day and every three hours at night. As there was no immediate response, a biopsy specimen was excised from one of the conjunctival nodules and at the same time a lymph node was removed. Histologically the specimen from the eye was a subepithelial accumulation of lymphocytes characteristic of a phlyctenule (Figure 3). In the specimen from the axillary lymph node, confluent areas of caseous necrosis had supplanted most of the normal structure. In the periphery there were numerous Langhans' giant cells and epithelial proliferation—the granuloma typical of tuberculosis. Acid-fast bacilli were present.

The patient was put at rest and treated with streptomycin and para-aminosalicylic acid. One new phlyctenule developed in the right eye and it responded readily to local application of cortisone.

DISCUSSION

The present case of tuberculosis with two manifestations of hypersensitivity, phlyctenulosis and vasculitis, was, except for phlyctenulosis, remarkably like a case recently reported by Gilrane and Cherry.[5] In that case a 30-year-old Caucasian who for 20 months was thought to have periarteritis nodosa was treated with cortisone for five months. Soon afterward a supraclavicular lymph node was noted, and biopsy and guinea pig inoculation proved it to be tuberculous. The diagnosis then was changed to tuberculous lymphadenitis and erythema nodosum simulating polyarteritis nodosa.

Rich[6] said that allergic reaction of anaphylactic type affects primarily smooth muscle and vascular endothelium. Gilrane and Cherry[5] commented upon the similar histologic picture and overlapping characteristics of polyarteritis nodosa, erythema nodosum, and other forms of allergic vasculitis. Polyarteritis nodosa is evidently a manifestation of hypersensitivity with a variety of causes. It has been classified in recent years as a "collagen disease." Erythema nodosum is also allergic vasculitis with a variety of causes, one of which is known to be tuberculosis, but it usually runs a milder course. It has not been classified as a "collagen disease."

Possibly because of the etiological relationship of hypersensitivity and the effect of cortisone and corticotropin on some of these diseases, the concept of collagen diseases has recently received much attention. However, an editorial in the *Journal of the American Medical Association* of September 20, 1952[3] warned that "undue significance should not be attached to the occurrence of fibrinoid changes in connective tissue collagen. Pathologically this is merely a form of degeneration, unspecified in etiology, that occurs in a wide variety of dissimilar diseases. This fact minimizes the clinical usefulness of the term *collagen disease*."

In the present case, current interest in the collagen disease concept may have led to early treatment with corticotropin and delayed the further investigations which finally brought to light the basic etiologic agent.

Although phlyctenulosis has been shown to be a hypersensitive reaction that can be evoked by a variety of antigens, it is clear that it is almost always an allergic manifestation of tuberculosis. Thygeson[7] expressed belief that the phlyctenule is comparable to the tuberculid of the skin. He noted that the incidence of phlyctenulosis has declined in parallel to the decline in tuberculosis in general; and that geographically the incidence is proportional to the local death rate from tuberculosis. Adler[1] said that it is most often associated with tuberculosis of lymph nodes and the decline in incidence is caused by the decline in tuberculosis of the bovine type due to improved sanitation of milk.

Phlyctenulosis is not infrequently precipitated in tuberculous persons by local staphylococcic infection and possibly by other antigens. It is known that animals sensitized by infection with the tubercle bacillus will react in an exaggerated manner to various unrelated bacteria and to certain non-bacterial proteins, a phenomenon that Rich[6] called *heteroallergy*. Phlyctenulosis was once known as eczematous keratoconjunctivitis because of the frequent coincidence of patches of eczema around the nose and mouth. Many observers have been impressed by the frequency of staphylococcic infection in the disease. Thygeson cultured coagulase-positive staphylococci from the conjunctiva and the margins of the eyelids of approximately half of a group of children with phlyctenulosis. He stated that "local bacterial infection appears to be a factor in precipitating the disease in predisposed individuals, but there is no valid evidence to indicate that the bacterial infection is ordinarily causal in itself." Rubert induced phlyctenulosis in tuberculous animals not only with tuberculin but also with

staphylococcic toxin. Guillary noted the same phenomenon in human beings.[8]

The patient in the present case had a pustular eczematoid eruption around the nose coincident with the appearance of tuberculous phlyctenules. It is probable that the organism causing the dermal lesion was the precipitating factor in a person sensitized by the tubercle bacillus—a "hetero-allergic reaction."

Phlyctenulosis should be considered tuberculous until proven otherwise. Management should never be limited to local treatment of the eye or to treatment during a single attack. A search should be made for active tuberculosis in the patient's environment.

SUMMARY

In a case of periarteritis nodosa or erythema nodosum the appearance of phlyctenules uncovered the agent causing allergic vasculitis.

The clinical and histologic characteristics of periarteritis nodosa, erythema nodosum and other forms of allergic vasculitis are overlapping. The advent of cortisone and corticotropin has greatly increased the need for differentiating cases of allergic vasculitis due to tuberculosis from those with other cause.

Phlyctenulosis is almost always an allergic reaction to the tubercle bacillus.

ACKNOWLEDGMENT

I wish to express my thanks to Dr. John B. Frerichs, Chief of Pathologic Anatomy, U.S. Veterans Administration Hospital, San Francisco, for preparation and interpretation of the histologic sections; and to Dr. Max Fine of Stanford University Medical School for his suggestions and advice.

REFERENCES

1. Adler, F. H.: Gifford's Text Book of Ophthalmology—4th ed., Saunders, Philadelphia, 1947.

2. Editorial: Cortisone, corticotropin, and tuberculosis, J.A.M.A., 149:1474-1475, Aug. 16, 1952.

3. Editorial: Collagen diseases, J.A.M.A., 150:220-221, Sept. 20, 1952.

4. Frerichs, John B.: Personal communication.

5. Gilrane, J. J., and Cherry, C. B.: Tuberculous mediastinal lymphadenitis and erythema nodosum simulating polyarteritis nodosa, Calif. Med., 77:34-36, July 1952.

6. Rich, A. R.: The Pathogenesis of Tuberculosis—2d ed., Thomas, Baltimore, 1951.

7. Thygeson, P.: Phlyctenular keratoconjunctivitis, Am. J. Ophthal., 34:1217-1236, Sept. 1951.

8. Urbach, E., and Gottlieb, P. M.: Allergy—2d ed., Grune & Stratton, New York, 1946.

California MEDICINE

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For information on preparation of manuscript, see advertising page 2

EDITORIAL

Training or Work?

SHOULD THE INTERN YEAR of medicine be considered an additional year of training or is it a period in which the newly graduated doctor performs professional services for a stipend?

This question is relatively new in medical education circles. It has arisen after many years of complete acceptance of the intern year as a year of study and training. And its arrival on the scene has caused reverberations which may take years to settle.

Medical training as we know it today follows a well-established pattern: the premedical years, the four years of medical school and the one year of internship. This last year has consistently been considered as a fifth year of medical school, a year of additional study under the tutelage of practicing physicians. The intern attends patients under the supervision of the attending physician and absorbs, in actual practice, the knowledge which in his earlier years of medical school was more theoretical in nature and not accompanied by personal responsibility.

As witness that the intern year is considered a period of instruction is the fact that some of our medical schools do not grant the M.D. degree until the student has successfully completed his internship. On top of that, many state licensing boards require a year of internship within the state, both as a means of measuring the training and skill of the applicant physician and of assuring his training in the practice of medicine as it is carried out within the state.

Within the past decade the number of approved internships became greater than the number of graduating medical students. When that occurred the value of interns as actual practicing physicians became apparent to hospitals and physicians throughout the country. Hospitals that had not theretofore offered internships found it convenient, if not actually a financial benefit, to set up internships and to use their interns for actual medical practice within the hospital.

In some instances there appears a reasonable question as to whether the intern was not actually performing services for which the hospital or someone else received a fee. If this were the case, the basic concept of the intern as a young doctor completing his medical education would, of course, be entirely lost.

Whatever the genesis of new internships, it is obvious that over the years the number of approved internships has grown out of bounds. In 1952 the A.M.A. Council on Education and Hospitals listed openings for interns which were more than double the number of candidates available.

The law of supply and demand then came into play and hospitals started bidding for interns. The old concept of an intern as a student, allowed "room, board, laundry and cigarette money," was washed into discard on the flood of lucrative offers advanced by some hospitals. In many instances the monthly stipend was more than even the most optimistic medical school senior had ever visioned in projecting himself into the world of interns.

The senior medical student was lured, with offers of cash, to accept an internship which would help establish him financially, or pay off debts, rather than a spot where his medical education could be furthered.

Today there is an even newer development in this field of auctioning off internships. Some closed panel medical care prepayment organizations have seized upon the availability of interns as means of supplying medical care, at a low cost, to the members of their prepayment groups who are entitled to medical or surgical service in their own hospitals. Where such groups have been able to secure approval of their hospitals for intern training, they are in an ideal position to use their interns as low-paid doc-

tors in caring for the beneficiary members of their prepayment plans.

While this development might not seem much of a departure from the intern situation of previous years, it is an economic fact that a prepayment plan in this position is able to bid more for an intern than other hospitals and yet less than it would have to pay for a graduate physician.

Thus the squeeze is put on the senior medical student, who may not have been thoroughly inculcated with the theory of the intern year as a training period. It is this very squeeze which caused the Advisory Committee to the Council on Medical Education and Hospitals to suggest methods of putting the brakes on the number of approved internships. A reasonable requirement that it fill a specified percentage of its approved internships should not harm any hospital which can attract interns through a recognized training program. At the same time, it should discourage the fringe hospitals which cannot attract house staffs on the basis of the training offered and so rely upon compensation to make up for the educational lack.

It is to be hoped that the nation's medical schools and hospitals will see the writing on the wall and will adjust their educational programs to the needs of the public and the medical students, rather than to the convenience of the institution or its attending staff.

LETTERS to the Editor . . .

Poliomyelitis Viremia

During the 1952 poliomyelitis epidemic three children in one Ohio family developed a mild illness, characterized by slight fever, anorexia, nausea, vomiting, headache and sore throat, in various combinations. This symptomatology is comparable with that of abortive poliomyelitis. All three children were completely recovered by the end of four to six days. A fourth child in the same family was without symptoms.

At the height of this brief illness of the three children, throat swabs, rectal swabs and blood specimens were collected from all four children. Horstmann and McCollum of Yale University cultivated and identified Type I poliomyelitis virus from each of the four blood specimens, and from all four throat and rectal swabs. The blood findings were similar to those recorded in orally infected chimpanzees and cynomolgus monkeys. In these animals viremia is noted several days before involvement of the central nervous system, suggesting a rapid preliminary multiplication of poliomyelitis virus outside the central nervous system, in the initial stage of the disease. Whether this initial multiplication occurs in neural or non-neural tissues, is under investigation.

REFERENCE

Horstmann, D. M., and McCollum, R. W.: Poliomyelitis virus in human blood during the "minor illness" and the asymptomatic infection, Proc. Soc. Exp. Biol. and Med., 82: 434, March 1953.

W. H. MANWARING, M.D.

Palo Alto, Calif.

California MEDICAL ASSOCIATION

NOTICES & REPORTS

Accident and Health Insurance For C.M.A. Members

MEMBERS OF THE California Medical Association are being offered a new group accident and health insurance policy which provides benefits greater than similar policies have previously contained.

Underwriter for this offering is the Lumbermens Mutual Casualty Co. of Chicago and administration is under the direction of Charles O. Finley & Co., brokers with offices in Chicago and other cities and California headquarters in Los Angeles.

The group policy provides a $5,000 benefit for accidental death and weekly benefits of $50 to $100 for disability from accident or illness. Total disability arising from accident will be compensated for lifetime, while disability from illness will be paid for a maximum of seven years. Most existing policies of this type limit the illness disability payments to periods of from two to five years. The seven-year disability period is believed to be the greatest ever offered in this type of contract.

Two types of policies are available under the group program. The first pays accident benefits from the first day and sickness benefits from the eighth day. The second pays both accident and sickness benefits from the thirty-first day and is correspondingly lower priced.

Weekly cash benefits are listed in amounts of $50, $75 and $100. Association members under the age of 60 may apply for any of these coverages, while those between 60 and 65 years may apply for the two lower coverages and those between 65 and 70 may secure only the $50 weekly benefit.

Provision is made in both types of policy for the payment of partial disability benefits, at half the regular weekly benefits, for partial disability arising from accident.

Disability payments will not require specified periods of attendance by a physician but regular attendance only. After six months of continuous disability, a waiver of premiums is effective. The plan is world-wide in coverage and includes regularly scheduled airline flying.

Hospitalization benefits to provide $70 weekly benefits for a period of three months are available at an additional premium cost.

The underwriter has agreed to accept all CMA members up to age 70, without recourse to a health statement, if 50 per cent of the Association's active membership signs up during the initial enrollment period. Should less than 50 per cent apply for the coverage, the underwriter could require health statements and base the issuance of policies on such statements.

Members above the age of 60 will not be accepted for this coverage after the charter enrollment period ends.

A series of mailings, including an announcement letter, a brochure, a specimen policy and a question-and-answer pamphlet, has been started by the underwriter and broker. This material is designed to answer all questions.

In the announcement letter, it was pointed out that this group coverage is not designed to supplant acci-

dent and health policies which members may already have through county medical societies, specialty organizations or hospital staffs. Rather, the CMA program is set up to supplement other coverages and to make possible a disability income more in keeping with professional income standards.

Laetrile

THE REPORT of the Cancer Commission on "Laetrile" of March 11, 1953, included a statement that the Butterworth Cancer Research Grants Inc., Los Angeles, had supported the investigation of Laetrile. Mr. A. A. Butterworth has informed the officers of the commission that this support was strictly in the nature of an outright grant of funds for the work which was being done on this agent by its proponents, and in no way indicated any sponsorship of Laetrile by the Butterworth family, whose own funds had set up a cancer research fund some time prior to the development of Laetrile.

The use of the names of the late Mrs. A. A. Butterworth, A. A. Butterworth or Albert W. Butterworth in the report of the Cancer Commission on "Laetrile" was not meant to imply that any member of the Butterworth family had a financial, managerial, promotional or ownership interest in "Laetrile."

The commission is happy to publish this information and also to emphasize that the listing of sources of support was not necessarily meant to imply sponsorship.

IAN G. MACDONALD, M.D.,
Chairman, Cancer Commission,
California Medical Association

Proposed Constitutional Amendment

(Second Publication)

Following is the proposed amendment to the Constitution of the California Medical Association that was introduced at the 1953 Annual Session and was carried over for action at the Interim Session. It has been referred to Reference Committee No. 4, which is to make its report upon it available to delegates at least 30 days before the opening of the 1953 Interim Session in San Francisco, December 12, 1953. California Medical Association members who wish to record opinions on the proposed amendment may send them to the chairman of Reference Committee No. 4, Albert G. Miller, M.D., 77 San Mateo Drive, San Mateo.

Submitted by Sidney J. Shipman, for the Council, May 24, 1953.

Resolved: That Article III, Part A, Section 1 of the Constitution of this Association, the California Medical Association, be amended by striking out the word "District" in subsection (c) of said Section 1, so that Section 1 will read as follows:

Section 1—Composition

"The House of Delegates shall consist of:

"(a) Delegates elected by the members of the component societies;

"(b) Officers of the Association as hereinafter provided;

"(c) Ex-officio, with the right to vote, the Councilors, and

"(d) Ex-officio, without the right to vote, the Past Presidents."

In Memoriam

BLEVINS, WILLIAM J. Died in Woodland, August 20, 1953, aged 82, of coronary occlusion. Graduate of the Barnes Medical College, St. Louis, Mo., 1898. Licensed in California in 1898. Doctor Blevins was a member of the Yolo County Medical Society, and a life member of the California Medical Association.

✤

BOBBITT, JAMES D. Died in San Diego, July 16, 1953, aged 68. Graduate of Rush Medical College, Chicago, Ill., 1911. Licensed in California in 1922. Doctor Bobbitt was a retired member of the San Diego County Medical Society.

✤

BRIDEN, VAYLE S. Died in Fresno, July 24, 1953, aged 44. Graduate of the State University of Iowa College of Medicine, Iowa City, 1936. Licensed in California in 1937. Doctor Briden was a member of the Fresno County Medical Society.

✤

CRANDALL, FRANK G., JR. Died in Hollywood, August 25, 1953, aged 57, of cerebral hemorrhage. Graduate of the University of Nebraska College of Medicine, Omaha, 1921. Licensed in California in 1927. Doctor Crandall was a member of the Los Angeles County Medical Association.

✤

CUNEO, PETER J. Died in Bakersfield, September 1, 1953, aged 68, of cerebral vascular accident. Graduate of Cooper Medical College, San Francisco, 1911. Licensed in California in 1911. Doctor Cuneo was a retired member of the Kern County Medical Society.

✤

DERBYSHIRE, ALBERT L. Died in San Francisco, September 5, 1953, aged 102. Graduate of the Medical College of Indiana, Indianapolis, 1886. Licensed in California in 1888. Doctor Derbyshire was a retired member of the Butte-Glenn Medical Society.

✤

FIDLER, ALBERT J. E., Commander, U.S.N. Died in Inyokern, June 12, 1953, aged 50, of injuries received in an automobile accident. Graduate of the St. Louis University School of Medicine, Missouri, 1929. Licensed in California in 1947. Doctor Fidler was a member of the San Diego County Medical Society, and an associate member of the California Medical Association.

✤

GIORDANO-CORTESE, MODESTO. Died August 18, 1953, near Yountville, aged 61, when his automobile struck a tree. Graduate of Regia Università di Napoli Facoltà di Medicine e Chirurgia, Italy, 1916. Licensed in California in 1931. Doctor Giordano was a member of the San Francisco Medical Society.

✤

GLATT, MORRIS A. Died in Los Angeles, July 18, 1953, aged 63, of cerebral hemorrhage. Graduate of the Stritch School of Medicine of Loyola University, Chicago, Ill., 1917. Licensed in California in 1946. Doctor Glatt was a member of the Los Angeles County Medical Association.

JOHNSON, KARL O. Died in Bakersfield, August 3, 1953, aged 41, of metastatic carcinoma of the testicle. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1942. Licensed in California in 1942. Doctor Johnson was a member of the Kern County Medical Society.

✤

LANG, JOHN H. Died in Fullerton, August 1, 1953, aged 71, of coronary artery disease. Graduate of the St. Louis University School of Medicine, Missouri, 1906. Licensed in California in 1910. Doctor Lang was a retired member of the Orange County Medical Association.

✤

LIPKIS, ABRAM. Died August 18, 1953, aged 78. Graduate of Denver and Gross College of Medicine, Colorado, 1907. Licensed in California in 1925. Doctor Lipkis was a member of the Los Angeles County Medical Association.

✤

LIVA, ARCANGELO. Died in Los Angeles, August 12, 1953, aged 66, of cerebral hemorrhage. Graduate of the Eclectic Medical College of the City of New York, 1912. Licensed in California in 1921. Doctor Liva was a member of the Los Angeles County Medical Association.

✤

MARSHALL, BENJAMIN. Died in Eureka, August 10, 1953, aged 77, of arteriosclerosis. Graduate of the College of Physicians and Surgeons of San Francisco, 1902. Licensed in California in 1903. Doctor Marshall was a member of the Humboldt County Medical Society, and a life member of the California Medical Association.

✤

SMITH, LORAN E. Died in Danville, August 23, 1953, aged 33, of injuries received when an automobile he was driving struck a tree. Graduate of the University of Illinois College of Medicine, Chicago, 1950. Licensed in California in 1951. Doctor Smith was an affiliate member of the Santa Clara County Medical Society.

✤

TURNER, HENRY C. Died July 19, 1953, aged 55. Graduate of the University of Virginia Department of Medicine, Charlottesville, 1947. Licensed in California in 1952. Doctor Turner was a member of the Los Angeles County Medical Association.

✤

WELLMAN, ORAND F. Died in San Pedro, August 5, 1953, aged 63. Graduate of the College of Physicians and Surgeons of San Francisco, 1922. Licensed in California in 1922. Doctor Wellman was a member of the Los Angeles County Medical Association.

✤

WESTPHAL, HENRY G. Died in Glendale, September 2, 1953, aged 72. Graduate of the American Medical Missionary College, Battle Creek, Mich., 1905. Licensed in California in 1918. Doctor Westphal was a member of the Los Angeles County Medical Association.

CALIFORNIA MEDICAL ASSOCIATION

Annual Meeting

LOS ANGELES
May 9-13, 1954

Papers for Presentation

If you have a paper that you would like to have considered for presentation, **it should be submitted to the appropriate section secretary** (see list on this page) not later than November 15, 1953.

Scientific Exhibits

The space available for scientific exhibits is limited. If you would like to apply for space, please write immediately to the office of the California Medical Association, 450 Sutter Street, San Francisco 8, for application forms. To be given consideration by the Committee on Scientific Work, the forms, completely filled out, must be in the office of the California Medical Association not later than December 1, 1953. (No exhibit shown in 1953, and no individual who had an exhibit at the 1953 session, will be eligible until 1955.)

SCIENTIFIC PAPERS . . .

. . . SCIENTIFIC EXHIBITS

PLANNING MAKES PERFECT

AN EARLY START HELPS

SECRETARIES OF SCIENTIFIC SECTIONS

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Anesthesiology . . . . . *Marshall L. Skaggs*
18 Hillcrest Road, Mill Valley

Dermatology and Syphilology . . *Walter F. Schwartz*
696 East Colorado Street, Pasadena 1

Eye, Ear, Nose and Throat—

Eye . . . . . *Alfred R. Robbins (Chairman)*
1930 Wilshire Boulevard, Los Angeles 57

ENT . . . . . *Francis A. Sooy*
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General Medicine . . . . . *Edgar Wayburn*
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General Practice . . . . . *Joseph W. Telford*
3255 Fourth Avenue, San Diego 3

General Surgery . . . . . *William Brock*
2633 Pacific Avenue, Stockton 4

Industrial Medicine and Surgery . . . . *Verne G. Ghormley (Asst. Secty.)*
2014 Tulare Street, Fresno

Obstetrics and Gynecology . . . *Charles T. Hayden*
411 Thirtieth Street, Oakland 9

Pathology and Bacteriology . . . . . *Paul Michael*
450 Thirtieth Street, Oakland 9

Pediatrics . . . . . *Gordon F. Williams*
1111 University Drive, Menlo Park

Psychiatry and Neurology . . . *George N. Thompson*
2010 Wilshire Boulevard, Los Angeles 57

Public Health . . . . . *L. S. Goerke*
116 Temple Street, Los Angeles 12

Radiology . . . . . *H. R. Morris*
1027 "D" Street, San Bernardino

Urology . . . . . *Thomas I. Buckley*
431 Thirtieth Street, Oakland 9

NEWS & NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

The fourth **Estelle Doheny Eye Foundation Lecture** will be delivered Thursday, November 5 at 8 p.m. in the Los Angeles County Medical Association Building. Dr. Frederick C. Cordes, clinical professor of ophthalmology at the University of California School of Medicine, San Francisco, will deliver the lecture. His subject will be "Endocrine Exophthalmos—an Evaluation."

* * *

The **Southern California Psychiatric Society,** a district branch of the American Psychiatric Association, will hold its annual meeting Saturday, November 14 at the Hotel Statler in Los Angeles. Guest speakers will be Douglass W. Orr, M.D., Seattle, Washington; Colonel Albert J. Glass, M.C., of the School of Military Neuropsychiatry, Fort Sam Houston, Texas; and Milton H. Erickson, M.D., Phoenix, Arizona. The meeting will consist of an afternoon scientific session and an evening cocktail party and dinner-dance. Physicians who are not members of the Southern California Psychiatric Society may register for the meeting as guests.

* * *

In an **exchange of faculty members** between the University of California School of Medicine, Los Angeles, and the University of Mexico School of Medicine, Dr. Justin Stein and Dr. Albert Bellamy of UCLA spent six weeks lecturing at the Mexican university and Dr. Albert P. Leon and Dr. Demetrio Sodi-Pallares came to UCLA for a like period. Drs. Bellamy and Stein lectured on the medical use of radioisotopes, Dr. Leon on infectious and parasitic diseases, and Dr. Sodi-Pallares on electrocardiography.

RIVERSIDE

The **American Society for the Study of Sterility** will hold a mid-annual regional meeting in Palm Springs, California, the week-end of November 6-8. Subjects covered in the formal presentations and panel discussions include among others: The role of surgery in infertility, prevention of sterility, artificial insemination and adoption, timing of ovulation, and the present status of treatment of the infertile male. Outstanding clinicians and investigators in the field of infertility will take part in the program. A major aspect of the meeting involves correlation of recent laboratory investigation with clinical problems.

Further program information may be had by communication with Dr. Edward Tyler, 10911 Weyburn Avenue, Los Angeles 24. Registration is open to all interested physicians and research workers, and may be made by addressing Dr. John O. Haman, 490 Post Street, San Francisco. The registration fee is five dollars. Hotel accommodations may be obtained by writing to the headquarters hotel, Deep-Well Ranch, or the Palm Springs Chamber of Commerce.

SAN DIEGO

The Seventh Annual Postgraduate Assembly of the **San Diego County General Hospital** was held September 23 and 24. Guest speakers were Dr. Thomas Findley, professor of clinical medicine, Tulane University; Dr. Joseph A. Weinberg, associate clinical professor of surgery, University of California at Los Angeles; Dr. Charles Higgins, chief of urology at the Cleveland Clinic; Dr. Verne Inman, professor of orthopedic surgery, University of California, San Francisco; Dr. Paul J. Moses, assistant clinical professor of otolaryngology, Stanford University School of Medicine; and Dr. Phil C. Schreier, professor of obstetrics and gynecology, University of Tennessee.

* * *

Announcement that **Dr. William Geistweit** had been made an honorary member of the San Diego County Medical Society, in recognition of 28 years of service in official capacity, was made at a meeting of the Society last month which was attended by officers of the California Medical Association. Dr. Geistweit was also presented with a scroll from C.M.A. memorializing his many years of service. He has been president of the county society, its secretary for more than 20 years, a delegate to the C.M.A. and chairman of many committees.

SAN JOAQUIN

Dr. C. A. Broaddus of Stockton, director of postgraduate activities of the California Medical Association, was elected secretary-treasurer of the State Medical Postgraduate Association at a meeting of that organization held last summer in New York City at the time of the annual convention of the American Medical Association.

GENERAL

The International Academy of Proctology has announced the establishment and award of a one-year **proctologic research fellowship** in the amount of $1200. This Research Fellowship grant has been awarded to the Jersey City Medical Center, New Jersey, to be administered under the direction of Dr. Earl J. Halligan, surgical director of the Medical Center.

Dr. Halligan is a former international president of the academy. The board of trustees of the International Academy of Proctology will vote another fellowship grant of a similar amount at the time of the next annual meeting of the academy.

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It is **illegal** for a clinical laboratory technologist or a clinical laboratory technician to perform **spinal punctures** in California, according to an opinion rendered by the office of the attorney general of the state. The opinion was given in response to a request by the California State Board of Medical Examiners for a ruling on the subject.

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The fifth annual **Symposium on Heart Disease** sponsored by the Washington State Heart Association and the Washington State Department of Health will be held November 6 and 7, 1953, in the auditorium of the University of Washington Medical School, Seattle. Dr. Herrman Blumgart of Boston, Dr. Howard Burchell of the Mayo Clinic, Dr. David Rutstein of Boston, and Dr. Paul Wood of London, will be guest speakers.

The symposium is the equivalent of nine hours of formal postgraduate training for members of the Academy of General Practice, it was announced.

* * *

The American Society for the Study of Sterility has announced the opening of the 1954 **essay contest** on the subject of infertility and sterility. The winner will receive

a cash award of one thousand dollars, and the essay will appear on the program of the 1954 meeting of the Society. Essays submitted in this competition must be received not later than March 1, 1954. Full particulars concerning requirements of this competition may be had from The American Society for the Study of Sterility, in care of Dr. Herbert H. Thomas, secretary, 920 South 19th Street, Birmingham, Alabama.

* * *

WHY, DOCTOR?—the **C.M.A.'s first television** show for Northern California—began Sunday, September 20, over KGO-TV (channel 7), the ABC station in San Francisco.

The 30-minute show featured commentary by three physicians from the Santa Clara County Medical Society on "The Perfect Machine." Doctors Henry C. Dahleen, Harold Y. Randle and J. Frederick Snyder discussed the human body and how the medical profession helps keep the machine running. Many visual aids were used throughout.

Dr. Douglas M. Kelley, professor of psychiatry and criminology at the University of California, is moderator of the programs which are presented every other Sunday at 6:00 p.m.

On October 11, WHY, DOCTOR? will present a discussion by three physicians, Doctors Ralph A. Reynolds of San Francisco, Lovell Langstroth of Oakland and Alf Haerem of San Mateo, on the problems of appetite and weight control.

On October 25, physicians from Sonoma, Napa and Solano counties will discuss allergy.

County medical societies throughout the Bay Area are cooperating with the C.M.A. in supplying physicians to appear on the programs.

A medical policy board passes on all material, and scripts are cleared by participating societies. Letters from listeners are referred to appropriate societies. The C.M.A.'s Public Relations Department is coordinating production, script writing and promotion of the public service programs.

POSTGRADUATE EDUCATION NOTICES

COLLEGE OF MEDICAL EVANGELISTS

Full-Time Basic Science Course in Surgery and Surgical Specialties

Date: October 5, 1953 through June 11, 1954.

Fee to be announced.

Contact: H. M. Walton, M.D., Chairman, Postgraduate Division, 312 North Boyle Avenue, Los Angeles 33.

RESEARCH STUDY CLUB OF LOS ANGELES

23rd Annual Clinical Convention of Ophthalmology and Otolaryngology

Date: January 18 through January 29, 1954. Each applicant must be a member in good standing of the American Medical Association in order to become eligible for attendance.

Fee: $100.00.

Contact: Pierre Violé, M.D., Treasurer, 1930 Wilshire Boulevard, Los Angeles 5, Calif.

UNIVERSITY OF CALIFORNIA AT LOS ANGELES

In Los Angeles

Annual Postgraduate Medical Seminar.

Date: September 28 to December 14, 1953.

Fee: $50.00.

Dermatology in General Practice (limited to 20 students).

Date: October 7-November 11.

Fee: $30.00.

Surgical Anatomy (limited to 30 students).

Date: November 5, 1953-January 27, 1954.

Fee: $75.00.

Dermatology Conference.

Date: February 11, 12, 1954.

Fee: $35.00.

Anesthesiology.

Date: Spring, 1954.

Fee: Details to be announced.

In Long Beach:

Techniques of Hypnosis (limited to 15 students).

Date: October 9, 1953.

Fee: $100.00.

In West Los Angeles:

Advanced Course Techniques and Application of Hypnosis (limited to 15 students).

Date: October 23, 1953.

Fee: $100.00.

Contact: Dr. Thomas H. Sternberg, Head of Postgraduate Instruction, Medical Extension, University of California, Los Angeles 24, California.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Ophthalmological Conference, University Extension Building, 540 Powell Street, San Francisco.

Date: December 2, 3, 4, 5, 1953.

Fee: $75.00.

Microscopy and Photomicrography.

Date: January 14 to June 3, 1954.

Contact: Office of Medical Extension, University of California School of Medicine, University of California Medical Center, San Francisco 22, California.

STOCKTON POSTGRADUATE STUDY CLUB

Fall Lecture Series, 1953

October 15—Recent Advances in the Practical Use of Hormones—Peter Forsham, M.D., University of California Hospital, San Francisco.

October 22—Diagnostic and Therapeutic Errors in the Handling of Tumors from the Standpoint of a Pathologist—Warren Bostick, M.D., University of California Hospital, San Francisco.

October 28—Differential Diagnosis of Urological Signs and Symptoms—Donald Smith, M.D., University of California Hospital, San Francisco.

November 12—Diagnosis and Treatment of Common Skin Diseases—Eugene M. Farber, M.D., Stanford Hospital, San Francisco.

November 19—Treatment of Infertility, Sterility and Habitual Abortion—Abraham R. Abarbanel, M.D., College of Medical Evangelists, Los Angeles.

SEMINARS OF THE ALUMNI COMMITTEE OF THE CHILDREN'S HOSPITAL, SAN FRANCISCO

Oct. 31, 1953—Naevi, Tumors and Malignancies in Childhood—10:00-4:30.

December 5, 1953—Surgery and Anesthesia in Childhood, with a discussion on the effects of hospitalization on the young child for surgical procedures.

January 23, 1954—The Problems of Prematurity and the Newborn Infant.

March 30, 1954—Acute and Chronic Infections and the Choice of Antibiotics in Treatment.

April 24, 1954—Childhood Ecology, with a discussion of physical, mental and emotional growth and development of the young child; the effects of deprivation of maternal care, and the impact of environment on the child.

A fee of $15.00 will be charged for attendance at all the seminars and those who wish to have further details or be on the mailing list for such details may write to: H. E. Thelander, M.D., Children's Hospital, 3700 California Street, San Francisco.

UNIVERSITY OF SOUTHERN CALIFORNIA SCHOOL OF MEDICINE

Diagnostic and Therapeutic Radiology—No. 858

Date: Course begins by arrangement.

Fee: 3 mos.—$250.00 6 mos.—$ 500.00
9 mos.—$750.00 12 mos.—$1,000.00

This course is designed for a limited number of qualified physicians who wish to prepare for the American Board of Radiology, and who wish specialized training in a particular field of medicine such as orthopedics, cardiology, etc. Course will be conducted in the Department of Radiology at the Los Angeles County Hospital. Course Directors: Ray A. Carter, M.D., George Jacobson, M.D.

Anesthesia

Date: Course begins by arrangement.

Fee: $300.00 (full time, three months).

Basic principles and techniques involved in administering the various anesthetic agents, including oxygen therapy and operating room care of patients. Open to a limited number of qualified physicians and dentists. Emphasis placed on practical administration of anesthetic agents. Presented at the Los Angeles County Hospital. Course Director: J. S. Denson, M.D.

Contact: Gordon E. Goodhart, M.D., University of Southern California School of Medicine, Division of Medical Extension Education, 1200 North State Street, Box 158, Los Angeles 33, California.

INFORMATION

Anxious Times in Tuberculosis*

EDGAR MAYER, *M.D.*, New York City

THERE IS A DANGEROUS TREND prevailing now in the profession at large, to belittle the magnitude of the tuberculosis problem. Indeed, even among physicians engaged in treating tuberculosis there is a deplorable lack of appreciation of the complexity of existing problems.

Present trends in tuberculosis indicate a phase so full of potentiality for good or evil that the question "whither tuberculosis" is no longer one of concern only to statisticians. Clinicians in daily touch with the problem cannot help speculating on current trends and their effects upon treatment of tuberculous patients. Study of current statistics arouses serious reflection regarding their significance and portent for the future. The full picture includes features with ominous potentialities. There are, indeed, some facts which indicate the possibly approaching critical recrudescence of morbidity with increased spread of the disease.

The persistently divergent trend in mortality and morbidity is one that should give us much concern. Recent statistical reports have derived therefrom a serious warning. The figures themselves are perhaps easier to explain by clinical trends than epidemiologic theories. Facts speak for themselves. Mortality from tuberculosis has by now reached the unprecedented low of 16 per 100,000. The downward trend in mortality from tuberculosis has recently become accelerated, and there is every reason to believe that this acceleration will continue. We may confidently expect that soon tuberculosis will cease to be a major cause of death.

This highly optimistic outlook in mortality stands in very sharp contrast with the pessimistic picture of morbidity. Recent statistics indicate that tuberculosis morbidity has tended to remain on a high level. It was recently pointed out by Drolet that morbidity figures for 1950 were higher than those for 1940 by more than 20 per cent.[1] The full implications of this trend were recently considered on the basis of latest morbidity figures, by Mary Dempsey, statistician of the National Tuberculosis Association.[2] In presenting the picture of "tuberculosis today" she paints a grim warning which we quote here in full: "The curious assumption on the part of some people that tuberculosis is no longer a major problem in the United States is not only at variance with the facts but is downright dangerous. Recent estimates place the number of Americans with tuberculosis, both active and inactive, at 1,200,000, a figure large enough to shake the hardiest optimist out of complacency.

"Approximately 400,000 active cases of the disease exist in this country, according to estimates agreed upon by the National Tuberculosis Association and the Public Health Service. Information on file in case registers indicates that of these 40,000 are sputum-positive patients living at home. An additional 75,000, also unhospitalized and with active disease, have not been medically examined during the past year. Add to the total of these two groups an estimated 150,000 unreported active cases, and we get an approximate 240,000 unhospitalized tuberculous Americans, most of whom are in a position to spread the disease. It becomes obvious, therefore, that tuberculosis is very much in the 'major problem' category."

It is natural for the clinician to associate the divergent trend of mortality and morbidity and persistent high morbidity levels with recent trends in the treatment and management of tuberculous patients. Consideration of trends in tuberculosis not only leads to a logical explanation of these trends but also foreshadows the ominous potentiality of an approaching critical phase.

Nothing is more obvious to the clinician than the fact that the recent acceleration in the decline of mortality can be attributed greatly to modern chemotherapy. Streptomycin has beyond question greatly reduced the incidence of fatal tuberculosis. The lifesaving effect of streptomycin has not been conclusively demonstrated in fatal hematogenous and miliary tuberculosis. On the other hand, however, since the great bulk of tuberculosis is pulmonary, here its effect at least for the time being is evident in the large numbers of lives saved. What the ultimate fate of these patients will be remains to be seen, and in their outcome may lie the answer to the question of persistently high morbidity.

It seems a paradox to speak of the potential dangers of recrudescence of disease in the present phase of tuberculosis, when we already have at our disposal a choice of several effective agents for its control. Yet this situation is the natural outgrowth of recent developments and rises from a human tendency toward overconfidence in our achievements

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The author is from the New York Post-Graduate Medical School.

and from relaxation of zeal and vigilance. The danger of a critical phase in tuberculosis is inherent in the following developments:

1. Overconfidence in the complete effectiveness of available chemotherapeutic agents has led to dangerous trends in the treatment of patients, in that

(a) more of them are now allowed to cure at home, and

(b) more of them are now treated with drugs in ambulatory fashion, while remaining under care of family physicians, without expert guidance of specialists. These trends make for wider contacts with potential spreaders of the disease.

2. Chemotherapy has resulted in an increased number of patients whose tuberculosis is of arrested, latent but potentially active, or reactivated status. This makes for an increased number of potential spreaders.

Overconfidence in the effectiveness of available drugs tends to blind us to the following facts: (1) By themselves these drugs singly or in combination will not bring about cure in the majority of patients. In a large proportion they result merely in suppression of activity or in temporary arrest or incomplete resolution with residues of potential activity. (2) Our criteria for recognizing latent activity are very inadequate. (3) Patients with lesions of latent activity tend to resist treatment.

It is remarkable how these developments tend to restore the very circumstances which have so long militated against our efforts to control tuberculosis, namely, our inability to bring under control cases of tuberculosis in their latent (incipient) phase. Before modern casefinding by x-ray surveys, the vast majority of new cases were not discovered before the disease had reached a far-advanced stage. Even now too many of the new cases are not discovered in the early phase. Incipient tuberculosis is latent tuberculosis, the activity of which is difficult to determine unless we have serial x-rays.

Today there are many patients whose lesions are latent because of recent chemotherapy. Only long-range observation will reveal whether or not they are healed. Resection of the potentially most dangerous lesions is now being performed in a number of these, and in a considerable proportion recrudescence of disease is a likelihood sooner or later.

Patients with latent tuberculosis have always evinced great resistance even to temporary separation from their work and families. Physicians treating these patients have always had to cope with this resistance. Overconfidence in drug therapy tends to augment this resistance of patients with an increased tendency on the part of physicians to yield. More patients with latent but potentially active disease accordingly will escape that close control in institutions under continuous expert surveillance which in recent years has been acknowledged an essential and important factor in tuberculosis control.

What about the recent epidemiologic shift of pulmonary tuberculosis to higher age groups? The majority of tuberculous patients, particularly males, are now found in the fourth and fifth decades. That which has been said above regarding clinical latency of the disease and resistance to institutional treatment applies particularly to these patients. Furthermore, an ever larger proportion of patients suffering from progressive pulmonary tuberculosis is in advanced age groups in which symptoms of their pulmonary disease tend to blend with symptoms of other diseases of advanced age. This further favors delayed recognition and limits energetic treatment of their tuberculosis.

All of the factors discussed above working together tend to bring about a weakening of tuberculosis control by a trend of events, one leading to the other through force of circumstances.

Last but not least the danger of streptomycin-resistant bacilli should be considered. There is a growing belief that long continued chemotherapy (with combined streptomycin and PAS) results in permanent loss of viability of the bacilli located in the lesions. This belief may ultimately prove to be wrong. If so we may face many recrudescences of tuberculosis by a flareup of (arrested) latent lesions with streptomycin-resistant bacilli. Even more ominous is the threat of an increasing number of new cases infected with streptomycin-resistant bacilli from the above described sources. Some workers now express faith in averting all this with BCG vaccination. This, too, appears to be dangerous overconfidence. An analysis by Drolet of recent reports from countries using BCG extensively since its introduction indicates no effect upon the trend of ratio of new cases.

Should the chain of events above discussed really lead to a recrudescence of tuberculosis, the consequences will then depend largely on the existence or absence of a curative, effective, chemotherapeutic agent. That the "INH" drugs are not such agents is quite apparent by now. Should we fail to develop another more effective drug are we not headed for a critical phase in tuberculosis?

REFERENCES

1. Drolet, G. J., and Lowell, A. M.: Dis. of Chest, 21:527, May 1952.

2. Dempsey, M.: Bull. Nat. Tuberc. Assn., 38:86, June 1952.

New Laws Affecting Medical Partnerships, Clinics and Auxiliary "Hospitals"

THE 1953 LEGISLATURE enacted three new laws that directly affect medical partnerships, clinics and industrial or emergency "hospitals."

The first measure, A.B. 459, amended the hospital licensing law by adding a new section prohibiting the use of the word "hospital" by any person unless the facility so designated is licensed by the State Department of Public Health, or unless the facility is one of the specially designated exempt institutions (federal and state hospitals, institutions relying entirely on prayer, mental institutions licensed by the Department of Mental Hygiene, infant shelters and homes for the aged licensed by the Department of Social Welfare, and county hospitals). Under this new law, it will be illegal to use the term "industrial hospital" or "emergency hospital" or the word "hospital" alone or in conjunction with any other words unless the facility is first duly licensed by the State Department of Public Health. Under the hospital licensing law the Department of Public Health does not issue a license until, after inspection, it is satisfied that the institution qualifies as a hospital and meets all the standards set forth in the hospital licensing law and department regulations.

The second measure is S.B. 1770, which completely revises the present clinic licensing law. S.B. 1770 does not become effective until January 1, 1954. Thereafter, however, clinics will be governed by the new clinic licensing law. The new law discontinues licensure for private pay clinics, except those already in existence. It defines charitable clinics, limiting licensed charitable clinics to bona fide charitable corporations; it continues the teaching and research classification; it provides for employers' clinics and employees' clinics, both of which must be operated on a nonprofit basis; outpatient departments of hospitals are exempt, inasmuch as the hospitals themselves must be licensed under the hospital licensing law; and the powers of the state to investigate applicants for a clinic license and to administer the law are clarified, with a specific outline of minimum standards. Violations of the clinic licensing law may be enjoined by court order, on application of the department. Most important of these changes in the clinic licensing law is the elimination after January 1, 1954, of the private pay clinic classification. For the future the use of the term "clinic" by newly organized groups or institutions will be limited to those clinics that are operated as charities or for teaching and research, or by an employer or a group of employees (limited to health services of such employees).

The third measure is S.B. 1349, which modifies the present sections of the Business and Professions Code (Bus. & Pro. Code Secs. 2393 and 2429) that forbid the use of any fictitious name by a physician in connection with his practice. The new law, which will be effective September 30, 1953, continues to prohibit practice under a fictitious name, but expressly permits the formation of medical partnerships, provided that if any such partnership or group does not use the names of all the partners in the conduct of its practice, then it must use at least the surname of one of the partners, plus the words "medical group." For example, if Doctors Black, White, Green, Brown and Gray form a group or partnership, they may designate themselves simply as "Doctors Black, White, Green, Brown and Gray." However, if they desire to use a shorter identification, they may call themselves the "Gray-Black Medical Group" or "Gray Medical Group," etc. As in the past, however, the practice of medicine and surgery under any fictitious or assumed name that does not identify one or more of the physician partners will constitute a violation of the Medical Practice Act.

The cumulative effect of the three new laws can be illustrated as follows: Dr. Brown may not identify his medical office as the "Emergency Hospital" or "Industrial Hospital" unless he qualifies for and obtains a hospital license from the State Department of Public Health. Dr. Brown may not identify his office as the "Silent Hills Clinic," nor may he obtain a license to operate a private pay clinic. Dr. Brown may, however, if he associates other physicians in partnership or association with him, identify the office in which he and his associates practice as the "Brown Medical Group," or *all* names of all physicians in the group may be used without embellishment.

The Chorionepithelioma Registry

Of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons

IT HAS BEEN about five years since the inauguration by the American Association of Obstetricians, Gynecologists and Abdominal Surgeons of the Albert Mathieu Chorionepithelioma Registry. The project was made possible by an initial monetary gift from the late Dr. Albert W. Holman, of Portland, as a memorial to his former colleague, the late Dr. Albert Mathieu, also of Portland. Later the financial support of the Registry came from the Association itself, and during 1952 from the American Cancer Society.

Beginning with January 1, 1953, the continuance of the Registry has been made possible by a gener-

ous annual grant made to the Association for this purpose by one of the strongest and most progressive specialty organizations of this country, the Obstetrical and Gynecological Assembly of Southern California, as a part of its various activities for the advancement of our knowledge of obstetrics and gynecology.

In 1947 an announcement of the formation of the Registry was made more or less simultaneously in the *American Journal of Obstetrics and Gynecology*, the *Western Journal of Surgery, Obstetrics and Gynecology*, the *Journal of the American Medical Association*, the *Archives of Pathology*, and the *American Journal of Pathology*. The purpose of the Registry, as stated in the original announcement, was the collection, authentication and study of chorionepitheliomas and such cognate material as hyatidiform moles. The frequent difficulties in diagnosis in this field, and the incompleteness and confusion in our knowledge concerning such lesions, were the primary incentives for founding the Registry. It has already become perhaps the richest storehouse of such material in the world, and at this writing the registered chorionepitheliomas alone number some 70 cases. As material accumulates and matures for follow-up purposes, publications based on the Registry material will be put out by the Registry Committee, which consists of Dr. Emil Novak, chairman, Baltimore, Md.; Dr. Willard C. Cooke, Galveston, Texas; Dr. Robert A. Ross, Chapel Hill, N. C.; and Dr. Herbert F. Schmitz, Chicago, Ill. The first of these publications will appear in the near future.

While many gynecologists, obstetricians and pathologists have already cooperated in this important work, it has seemed wise to bring the Registry again to the attention of the profession, and to seek for even wider and more general cooperation. Clinical data, together with representative slides or gross tissue, may be sent to the chairman, Dr. Emil Novak, at 26 East Preston Street, Baltimore 2, Md. Regular printed forms for systematizing clinical histories are obtainable from the chairman of the committee. While the Registry makes no pretense of conducting a rapid diagnostic service, prompt acknowledgment of the material will be accompanied by the purely personal diagnostic impression of the chairman, with the explanation that the material will be circulated among all members of the committee for more deliberate collective study before final classification.

Both the sponsoring organization, the American Association, and the Southern California Assembly, which has so generously committed itself to the support of the Registry, invite the cooperation of the profession in this potentially rich investigative project.

N. J. EASTMAN, M.D.
President, American Association Obstetricians, Gynecologists and Abdominal Surgeons

EMIL NOVAK, M.D.
Chairman, Chorionepithelioma Committee

THE PHYSICIAN'S *Bookshelf*

THE PHYSICIAN IN ATOMIC DEFENSE — Atomic Principles, Biologic Reaction and Organization for Medical Defense. Thad P. Sears, M.D., F.A.C.P., Associate Clinical Professor of Medicine, University of Colorado School of Medicine. The Year Book Publishers, Inc., Chicago, 1953. 308 pages, $6.00.

This book has been very well written and should serve as a valuable source of information for all physicians as well as radiologists particularly in regard to the medical aspects of the atomic bomb and of the place of the physician in civil defense activities. Although the book contains a great deal of scientific information these data have been presented in such a manner that physicians without a background in radiological physics can easily follow the text. It is highly probable that cities will be the front lines of defense in the next war and a great deal of the responsibility will have to be borne by physicians and for that reason it is necessary that physicians and citizens learn as much as possible about civilian defense.

The table of contents of the book is as follows:

Section I—Atomic Theory, Basic Physics, and Atomic Bombs.

Section II—Clinical, Biologic, Pathologic and Therapeutic Aspects of Atomic Warfare.

Section III—Organization of the Medical Department for Atomic Defense. A great deal of discussion has been presented to cover all phases of the role of the physician in atomic defense. The general knowledge of the physician will also be enhanced by the discussions on the basic physics of radioactivity, isotopes, nuclear fission, phenomenology and hazards of atomic bomb bursts, methods of protection against radioactive materials, et cetera.

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DIURETIC THERAPY—The Pharmacology of Diuretic Agents and the Clinical Management of the Edematous Patient. Alfred Vogl, M.D., Assistant Professor of Clinical Medicine, New York University College of Medicine. The Williams and Wilkins Company, Baltimore, 1953. 248 pages, $5.00.

From his own wide experience and from an extensive bibliography, the author has produced this monograph which merits not only the acclaim of the medical bibliophile but also the acceptance and approval of the practitioner of medicine. Although the reader will enjoy the clarity by which the subject matter is presented, he will not read it without converting the information which is presented into practical use.

Based upon concepts which are included in a brief introductory chapter in which edema is classified and its pathogenesis and principles of treatment are clearly identified, the two successive chapters, one on the indications for diuretic treatment and the other on the pharmacology of diuretic drugs, lay a foundation for a clear understanding of the material presented in the following chapters which identify the selection and use of diuretic agents. One is not left with an ill-defined or isolated concept of diuretic drugs because other factors which are pertinent to the cause of edema and its possible elimination are so well integrated.

In his closing remarks, the author states his hope that "this book may contribute to making these achievements more easily available to the man who represents the vital link between scientific progress and suffering patients, the medical practitioner." It is the opinion of this reviewer that the hopes of the author will be realized quickly when the instructions given in this book, which the writer of the foreword calls "both scholarly and practical," are put to use.

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HEADACHES—Their Nature and Treatment. Stewart Wolf, M.D., Professor and Head of the Department of Medicine, University of Oklahoma School of Medicine; and Harold G. Wolff, M.D., Professor of Medicine (Neurology), Cornell University Medical College. Little, Brown and Company, 34 Beacon St., Boston, Mass., 1953. 177 pages, $2.50.

This small book, intended for the layman who wants to gain an understanding of the mechanism of headache, can be read to advantage by the practitioner who is not willing to devote the time to the perusal of the many papers on the subject by the authors. Just what place such a book for the laity has is open to question. Although the statement is made repeatedly that the book in no way takes the place of the physician, and that its suggestions should be followed only after thorough professional examination, there are bound to be many individuals who will use it as a substitute for the medical work-up, possibly with untoward results. On the other hand, the physician can make good use of the book by recommending it to the more intelligent of his patients who suffer from headache of non-organic nature. Although an attempt has been made by the authors to avoid technical terminology, a glossary of such terms would have been an asset.

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DIAGNOSTIC TESTS IN NEUROLOGY. Robert Wartenberg, M.D. The Year Book Publishers, Inc., Chicago, 1953. 228 pages, $4.50.

This small volume is devoted to physical signs of neurological disease that may be elicited at the bedside without special apparatus or laboratory aids. Furthermore, it presents a plea for greater stress on such physical diagnostic methods in modern practice. Certainly no one can find fault with this reasoning, although the present-day trend is quite in the opposite direction.

The author has carried on for many years a fight against the use of eponyms in description of neurological signs and syndromes, and this is carried on in this book. Whether anything is accomplished by substituting for the short term Romberg the appellation "feet together eyes closed test" is open to debate.

Many of the tests described are of more interest to the experienced and curious neurologist than to the student or

general practitioner interested in doing the briefest neurological examination consistent with a reasonable degree of thoroughness. It by no means takes the place of one of the short treatises on neurological examination already available. It does, however, make very interesting reading for the neurologist, particularly if he is acquainted with the author, who is able to inject much of his personality into the text.

* * *

THE LIVING BRAIN. W. Grey Walter. W. W. Norton and Company, Inc., 1953. 311 pages, $3.95.

Here is a book that should be read by every physician. Ostensibly written for the layman, it is not easy reading even for one trained in neurophysiology; yet the content is such as to make it very worthwhile reading. The author has been a pioneer in the field of electroencephalography, to which he brought the viewpoint of the physical scientist rather than the physiologist. The present work is an example of how much the physical sciences have contributed to the production of a theory of mental processes which, although far from complete, at least has a basis understandable without recourse to things metaphysical. The book comprises a consideration of the evolution of the nervous system, and an effort to explain, on a basis of Pavlov's elucidation of the conditioned reflex and knowledge gained from electrophysiology and electronics, how the human brain works as a thinking machine. How well the author has succeeded in this task must be left to the reader; the attempt, however, is provocative and worthy of thought. It is possible that the lay reader could sit down and read the book through in an evening as an interesting variant from science fiction; to one versed in the field of electrophysiology it contains an ample ration for an extended period.

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SYMPATHETIC CONTROL OF HUMAN BLOOD VESSELS. H. Barcroft, M.A., M.D., M.R.C.P., Professor of Physiology, St. Thomas's Hospital Medical School, formerly Dunville Professor of Physiology, Queens' University, Belfast; and H. J. C. Swan, Ph.D., M.B., B.S., F.R.C.P., formerly Lecturer in Physiology, St. Thomas's Hospital Medical School, Research Associate, Mayo Foundation. Distributed by Williams and Wilkins Company, Baltimore, for Edward Arnold & Co., London, 1953. 165 pages, $3.75.

This small volume summarizes clearly the modern concepts of sympathetic control of blood vessels. Most of the work on which it is based was performed by its authors on human subjects, with current techniques and the classical understanding of British physiologists at their best. Chapters on noradrenaline, adrenergic blockade, pheochrome tumors and vasovagal fainting deserve special mention; there is an appendix on plethysmography. The work is highly recommended.

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HOW TO IMPROVE YOUR SIGHT—Simple Daily Drills in Relaxation—Revised Edition. Margaret Darst Corbett (authorized Instructor of the Bates Method). Crown Publishers, Inc., 419 Fourth Ave., New York, 1953. 93 pages, $1.50.

This book is a revised edition of instructions on use of the Bates Method of correction of "eye troubles" by "scientific relaxation." It is divided into 15 chapters, each averaging five pages. The author conducts the School of Eye Education for which the book is the standard text. On the inside of the dust cover it is said that, "The sight-improvement of Dr. William H. Bates was once considered revolutionary: Today it is the one irrefutable, simple, scientific yet commonsense theory known throughout the world."

The book contains many statements that cannot be subscribed to on the basis of modern scientific ophthalmology. For example: "The extrinsic muscles, not the lens, used correctly, make accommodation." Again: "Serious conditions of the eye, formerly considered hopeless, such as atrophy, glaucoma, cataract, sympathetic ophthalmia and even detachment and hemorrhage, may often be improved by relaxation, if there is any vision left at all with which to work and if the method is practiced a sufficient length of time."

A great deal of emphasis has been placed on the value of the Bates Method in the treatment of myopia. Two extensive series have been studied in this country, one at Washington University and the other at the Wilmer Institute of Johns Hopkins. The conclusions of both were similar, and can best be summarized by quoting the last sentence of the Wilmer report which was based on a study of 103 patients given a course of visual training by a group of optometrists and psychologists:

"With the possible exception of educating some patients to interpret blurred retinal images more carefully and of convincing some others they could see better even though there was no actual improvement, this study indicates that the visual training used on these patients was of no value for the treatment of myopia."

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DERMATOLOGY IN GENERAL PRACTICE. Jacob Hyams Swartz, M.D., Assistant Professor of Dermatology, Harvard Medical School. The Williams and Wilkins Company, Baltimore, 1953. 581 pages, $11.00.

This volume can be highly recommended for the general physician. It has certain features which he will find very helpful. The most important is the topographical arrangement under which he can refer to a certain area of the body and find out which dermatoses most frequently occur there; for example, erythema nodosum on the shins. Another valued item consists of specific instructions for applying methods of treatment; for example, the way to give a carbolic shampoo for head lice. The book is full of such valuable everyday details.

The photographs are, in general, good but could be made much more instructive if they were in color. The chapter on the exanthemata is too brief and devoid of photographs. The chapter on syphilis is brief but is well illustrated and gives sound advice on therapy.

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THE CIBA COLLECTION OF MEDICAL ILLUSTRATIONS — Volume 1 — Nervous System. Frank H. Netter, M.D., commissioned and published by the Ciba Pharmaceutical Products, Inc., Summit, N. J., 1953. 143 pages, 104 full-color paintings, sold at cost, $6.00.

The material in this volume has already come in serial form to the office of most physicians as part of the advertising policy of the pharmaceutical company publishing it. Dr. Netter's drawings pertaining to the nervous system are now assembled, together with the text composed by outstanding authorities.

This book is directed to the clinician whose interest and contact with matters neurological is occasional, and who therefore may require some ready neuroanatomic reference to help in the general localization of central nervous system lesions, or to remind him of the fundamental characteristics of some of the more common of these diseases.

The artist has stated his intent to avoid "minute details and controversial theories," and "to compress" in these drawings "the most important and clinically useful facts" pertaining to the anatomy and, to a less degree, the physiology of the nervous system. The details have been eliminated as planned, and considerable information of clinical value may be obtained from the work of the artist and his

collaborators (not named on the title page). However, in any abridged presentation of a subject, the omission of topics or the absence of qualifications may lead to misconceptions. This volume is no exception to the rule. Dr. Netter has not avoided the controversial as well as he may believe. For example, the plate presenting the localization of function of the cerebral cortex includes "suppressor" areas whose very existence in the human cortex—let alone their exact location—has yet to be demonstrated unequivocally. This is known to the specialist in the field but may not be recognized by the practitioner for whom the drawing is made. Unfortunately, there are a number of similar situations in other plates.

In general, however, the non-specialist will find the book helpful and, in most instances, sufficiently accurate for his needs. Its use, however, should include its text as well as its illustrations.

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AN ATLAS OF THE COMMONER SKIN DISEASES—4th Edition. Henry C. G. Semon, M.A., D.M.(Oxon.), F.R.C.P. (London), Consulting Physician for Diseases of the Skin and Former Lecturer to Postgraduates, Royal Northern Hospital. With 147 plates reproduced by direct colour photography from the living subject. The Williams and Wilkins Company, Baltimore, 1953. 371 pages, $13.50.

By combining colored photographs of the various dermatoses with a clinical description of each case, along with appropriate therapy thereof, this volume takes a step in the right direction, as a standard textbook of dermatology with all of the illustrations in color is badly needed.

The photographs in color are, in general, good. The clinical discussions are excellent. The therapeutic recommendations are sound, but unfortunately do not include some of the newer antibiotics for local use only, such as neomycin and bacitracin, for the management of the pyogenic skin diseases, and there is no mention of the great value of ACTH and cortisone in such serious diseases as pemphigus vulgaris. It is possible that these remedies were not available when the text was prepared.

* * *

CLINICAL CARDIOLOGY. Edited by Franklin C. Massey, A.B., M.D., Assistant Professor of Medicine, Hahnemann Medical College, Philadelphia. The Williams and Wilkins Company, Baltimore, 1953. 1,100 pages, $13.50.

This impressive volume, under the editorship of Dr. Massey, represents the work of 33 authors covering the field of heart disease. Within the last few years so many new books and new editions of works dealing with the various aspects of diagnosis and treatment of cardiac disease appeared in print that it is almost customary for the author to apologize for writing another book and to state his reasons for doing so. Dr. Massey makes two points in his preface: One, that hitherto inadequate space has been devoted to some "specialty problems" such as pediatrics, anesthesiology, obstetrics and psychiatry in connection with heart disease. He states, furthermore, that the presentation of some newer data usually takes an unnecessarily long time to appear in textbooks, and that controversial subjects are often omitted. In line with these views one finds several chapters which are usually not included in texts on heart disease; separate sections on anatomy of the heart, physiology of the heart; psychiatric implications of cardiology, etc.

Other chapters follow a conventional pattern; general discussions on the normal heart, on cardiac roentgenology and electrocardiography, followed by chapters presenting various cardiac disease entities, such as rheumatic heart disease, hypertension, endocarditis, pericarditis, and others. One whole chapter (15 pp.) is devoted to "tumors of the heart and pericardium." Two chapters are devoted to cardiac therapy: treatment of arrhythmias and of congestive failure.

While books with multiple authorship offer many advantages, primarily the opportunity for presenting discussion of various subjects by experts in the field, there are well-known disadvantages which are illustrated in this book. Such are: The uneven presentation of various topics with overly lengthy presentation of some and too brief discussion of others; the overlapping and omission of various problems; and the difference in readability of the various presentations. Two chapters impressed the reviewer as unduly long: That on cardiac surgery (100 pp. or ten per cent of the book) which contains not only detailed differential diagnosis of various congenital cardiac defects (which are also discussed in other chapters) but also many minutiae of surgical technique. The other chapter in which the long discussion probably transgresses the line of interest of the average cardiologist is that on arteriosclerosis which deals primarily with the theoretical aspects of its pathogenesis and is 68 pages long. In comparison, it is noteworthy that the subject of rheumatic heart disease *and* rheumatic fever is presented jointly in a 40-page section, and an equal amount of space is devoted to the therapy of cardiac failure. Treatment of hypertension is discussed in eight pages. The section on electrocardiography impresses one as too advanced for the average clinician; the one on roentgenology appears rather elementary.

In spite of these criticisms the book represents a great deal of thought and planning on the part of the editors and a wealth of valuable information. It provides interesting reading to the advanced student, the internist and the cardiologist, and can be recommended. It does not, however, provide enough unusual and original aspects to put it above the average textbook of cardiac disease. Furthermore, the emphasis on up-to-the-minute presentation of current views and on controversial points is hard to evaluate at the present time; it may prove to be an asset but it may turn into a liability by making the book outdated in a relatively short time.

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DISEASES OF CHILDREN—Garrod, Batten and Thursfield—In Two Volumes—Fifth Edition. Edited by Alan Moncrief, C.B.E., M.D., F.R.C.P., Nuffield Professor of Child Health, University of London; and Philip Evans, M.D., F.R.C.P., M.Sc., Physician to the Children's Department and Director of the Department of Child Health, Guy's Hospital. Edward Arnold and Co., London, 1953. Distributed by Williams and Wilkins Company, Baltimore. 1973 pages, $21.00.

This is a new and thoroughly revised edition of the English text originally edited by Garrod, Batten and Thursfield. The present edition is the fifth—the preceding one having appeared in 1947. The editors are Professor Alan Moncrief and Dr. Philip Evans of the Hospital for Sick Children at Great Ormond Street and Guy's Hospital, both in London. The 50 contributors are drawn from all of Great Britain—half of them from the staff of the Hospital for Sick Children.

Besides covering the field of pediatrics in a thorough and competent manner, the text is profusely illustrated and, in addition, provides up-to-date references. These are chiefly concerned with the European literature and, as such, provide valuable source material frequently not mentioned in American texts. These two volumes are recommended to pediatricians, and to those whose practice includes a large share of children, as a valuable supplement to American texts.

ROENTGEN, RADIUM AND RADIOISOTOPE THERAPY. A. J. Delario, M.D., member of the American College of Radiology; American Board of Radiology; Head of Therapeutic Radiology, St. Joseph Hospital, Paterson, N. J. Lea & Febiger, 1953. 371 pages, 65 illustrations, 155 tables, $7.50.

The practice of clinical radiology, like other forms of medicine and surgery, involves both art and science. The scientific part is compounded of various portions of Physics, Chemistry, Physiology, Pharmacology and so forth. This interesting little book stresses principally the physical aspects of the field of therapeutic radiology.

After chapters on the composition of matter, the production of ionizing radiation and the nature of roentgen rays, there are sections dealing with methods of measuring ionizing radiation and a discussion of the physical factors involved in tissue ionization. The author discusses the biological changes produced by radiation, the erythema dose, the recovery of tissue from radiation and the types of injury caused by ionizing radiation. Along with conventional roentgen and radium rays, he discusses ultra-high voltage radiations, radioactive isotopes and other modalities.

As a result of his preoccupation with physical measurements, the sections on recommended clinical radiation dosage tend to be brief and therefore arbitrary. If human tissues, and especially human tumors were standardized, many of the dosage figures he gives would probably be of considerable value. However, each tumor is a law almost unto itself, and is surrounded by a host of highly variable biologic nature. As a result the effective dose for tumor A in patient B may be somewhat different from the effective dose for tumor B in patient A. Nevertheless, the galaxy of facts of interest to radiologists, and those concerned with radiation effects, which the author has assembled into one convenient place, is to be commended. He is chief of the therapeutic radiology division of St. Joseph's Hospital in Paterson, New Jersey.

There is a bibliography of over three hundred references and an adequate index.

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POLIOMYELITIS. W. Ritchie Russell, C.B.E., M.D. (Edin.), M.A. (Oxon.), F.R.C.P. (Edin.), F.R.C.P. (Lond.), Consultant Neurologist to the United Oxford Hospitals, Consultant Neurologist to the Army, Clinical Lecturer in Neurology, University of Oxford. Williams and Wilkins Company, Baltimore, 1952. 84 pages, $3.00.

This book presents a review of the literature, largely American in origin, in the form of a relatively short dissertation on the causes, epidemiology, diagnosis, and treatment of poliomyelitis. The section on differential diagnosis is lamentably weak, and the treatment offers nothing that is new, and much that we believe to be in error, such as prolonged postural (head-down position) drainage, which has been proven to impair respiration after 15 minutes in patients suffering from severe respiratory inadequacy, due to the weight of the abdominal viscera on the diaphragm.

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THE PHYSICAL EXAMINATION OF THE SURGICAL PATIENT. J. Englebert Dunphy, M.D., F.A.C.S., Associate Clinical Professor of Surgery, Harvard Medical School; and Thomas W. Botsford, M.D., F.A.C.S., Clinical Associate in Surgery, Harvard Medical School. W. B. Saunders Company, Philadelphia, 1953. 326 pages with 188 figures, $7.50.

As the authors state in the preface, this book is designed to focus attention on the methods and importance of eliciting signs in surgical conditions. It is a timely book for this age, in which it has become so popular to rely exclusively on myriads of laboratory tests for a diagnosis. The authors have written in a clear and concise manner, and have covered thoroughly the methods of performing a physical examination of various organs and what one might expect to see, feel and hear in the various surgical diseases. The book is divided into two parts, each with subdivisions by systems or organs. The first part is designated "the elective examination," and the second part "the emergency examination." It is particularly recommended for the younger generation who seem to depend entirely too much upon the laboratory for a diagnosis.

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HANDBOOK OF TREATMENT OF ACUTE POISONING. E. H. Bensley, M.B.E., B.A., M.D., F.A.C.P., Director, Department of Metabolism and Toxicology, Montreal General Hospital; and Associate Professor of Experimental Medicine & Lecturer in Toxicology, McGill University; and G. E. Joron, B.A., M.D., C.M., Dip.Int.Med., Demonstrator in Medicine, McGill University and Junior Assistant, Department of Medicine, Montreal General Hospital. Renouf Publishing Company, Ltd., 2182 St. Catherine St. W., Montreal 25, Que., Canada. 201 pages, $2.50.

A book so small that it can be conveniently placed in the pocket or in the physician's bag, with up-to-date and complete information on the treatment of poisoning is the thing to be desired. This book accomplishes these requirements to an unusual extent. It contains but 200 pages, is 4½x7 inches in dimensions, gives the principal symptoms and signs of poisoning by most of the substances encountered in a medical practice outside of industrial medicine and lists in one, two, three order the first aid treatment to be carried out by the physician. Basic principles are discussed in the 35 pages of section 1. The fact that reasons for specific symptoms and treatments are not discussed does not detract from the value of this book as a quick reference for what to do when.

A distinct lack is the treatment of poisoning by insecticides, other than the organic phosphate cholinesterase inhibitors. It is obvious that the authors have had practical experience in the field of toxicology. For example, they emphasize oxygen administration even in the absence of frank cyanosis in poisoning by depressant drugs and they wisely advise preventing overdistention of the urinary bladder, and watching for signs of bronchopneumonia. The reviewer takes issue with two items of treatment; dilute permanganate solution is frequently advocated, contrary to present evidence that it is of little value, and probably dangerous, and ethyl alcohol is advocated in methyl alcohol poisoning. It has recently been shown that although theoretically there may be a metabolic antagonism between these two alcohols, there is no therapeutic antagonism.

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FOOL'S HAVEN. C. C. Cawley. House of Edinboro, 21 Edinboro Street, Boston 11, 1953. 238 pages, $2.75.

Death from reliance on faith and prayer is the theme of this novel. The hero, a Caltech student, falls in love with his landlady's daughter, a high school senior. Their marriage is set for two days after her graduation but is cancelled by her death.

Throughout the courtship the hero realizes that the girl's mother is fanatically religious and has carried her daughter and younger son along with her. The mother bases her reliance on prayer on the fact that doctors had failed to save her husband's life and that a neighbor's son had been operated on for appendicitis and had died. The facts that her husband's disease was incurable and that the neighbor's son had been kept from medical attention until too late do not impress her. The pastor of her church, a self-ordained minister, does impress her and she places herself and her family in his hands and those of the church elders.

When death, aided by a ruptured appendix, does take the daughter, the mother recants none of her philosophy

but stands trial for manslaughter. She is convicted but her pastor, also a defendant, is found not guilty because he has no legal obligation to provide medical care for the girl. The mother is then granted probation and thus goes on her own way with her teenage son.

The author strives to make out a case against the church pastor as an accessory before the fact and, therefore, equally guilty in the girl's death. Morally, his case might stand; legally, it falls short. This book may be used as an "Uncle Tom's Cabin" for those who would find church leaders equally guilty with parents where the lives of minor children are in jeopardy. However, with our constitutional guarantee of freedom of religion, it is doubtful that the moral the author presses will find public, or least, court acceptance.

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THE LOW SODIUM COOK BOOK. Alma Smith Payne, M.A., and Dorothy Callahan, B.S., Research Dietitian, Massachusetts General Hospital. Little, Brown and Company, Boston, 1953. 477 pages, $4.00.

This is an excellent cook book, which also may serve as a textbook, for the patient on a low-sodium diet. The authors have thoroughly informed themselves on their subject, and they tackle the problem of the low-sodium dieter with expertness, good sense and humor.

They have developed many appetizing and interesting recipes and menus—leaning on herbs and wines for seasoning—and they present these with calculation of the sodium, fat and calorie values. There are also appendices which include tables of the sodium, cholesterol and fat content of common foods, sources of commercial low sodium products and the sodium content of public water supplies.

The book is written in a readable, lively style, and should prove especially encouraging to the patient or the family first confronted with the rigors of low-sodium dieting. It sets a standard which should be emulated in other fields of special diets.

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HYPERSPLENISM AND SURGERY OF THE SPLEEN. William Dameshek, M.D., and C. Stuart Welch, M.D., Pratt Diagnostic Hospital, New England Center Hospital and Tufts Medical College Medical School, Boston. Grune and Stratton, Inc., New York, 1953. 84 pages, $10.00.

This book is an extension of Dameshek and Estren's *Spleen and Hypersplenism*, published in 1948, to which has been added a section of surgery of the spleen by C. Stuart Welch, M.D. The material is presented chiefly in graphic form, being adapted from a prize-winning A.M.A. exhibit in 1950. It is hand lettered, printed on heavy paper and bound by a plastic ring. There are numerous illustrations, many in color, which probably account in part for the unusual cost for a volume of so few pages. Three-fourths of the book is devoted to the spleen and its diseases, with consideration of its anatomy and physiology. The different disease states are discussed and illustrative cases are presented. Emphasis is placed on Dameshek's concept of hypersplenism as a disorder resulting from marrow inhibition by humoral regulation. Treatment is discussed, and their reported results with ACTH and cortisone therapy in immunogenic hemolytic anemia are much better than those generally obtained elsewhere. One-fourth of the book is devoted to surgery of the spleen, the indications and technique, with consideration even of portacaval shunt. There is much repetition and oversimplification of the material throughout the book, which would be of most value to medical students, general practitioners and beginners in the field of hematology.

SPLEEN PUNCTURE. Sven Moeschlin, Privatdozent, University Medical Clinic, Zurich. Translated by A. Piney, M.D., Grune and Stratton, New York, 1951. 229 pages, $5.50.

This small volume is the outstanding work on spleen puncture. As in other fields of endeavor, when an individual devotes himself to a particular problem, in Moeschlin's hands, spleen puncture is a simple and valuable procedure. Moeschlin has had no mortality and little morbidity in hundreds of cases, in contrast to the results in the few small series reported from this country. In his book, he gives careful instructions as to the technique of spleen puncture, and the reviewer, having seen the author in action, can confirm its simplicity. The normal and abnormal cell pictures of the spleen are discussed, and there are many fine illustrations, both black-and-white and color. The last three-quarters of the book are devoted to detailed descriptions of the "splenogram" in a great variety of disorders involving the spleen. While splenic puncture can be dangerous and of no value to the uninitiated, this book should be available for reference to all hematologists and pathologists.

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OPHTHALMIC SURGERY — 6th Revised Edition — A Handbook of Surgical Operations on the Eyeball and Its Appendages. J. Meller. Revised by Professor J. Bock; translated and edited by Ray K. Daily, M.D., F.A.C.S., and Louis Daily, Jr., B.S., M.D., Ph.D. (Ophth.), F.A.C.S. The Blakiston Company, New York, 1953. 529 pages, $12.00.

Meller's Ophthalmic Surgery has long been a classic and it has been many years since the English edition has been available to Americans. The sixth edition of the original in German was revised and enlarged by Professor J. Böck, a former student of Meller's. In revising it he has kept the original material of Meller which is applicable to modern surgery and brought the book up to date without destroying its character. The illustrations are clear cut and easily understood. In looking at them, however, it must be remembered that they are drawn from the viewpoint of the Viennese operator who always sits to the patient's right side.

The English translation by the Dailys (mother and son) has been very well done. There is some doubt whether the appendix by the translators adds sufficient to warrant its inclusion in the book. The book contains an excellent index

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SYMPTOMS AND SIGNS IN CLINICAL MEDICINE—An Introduction to Medical Diagnosis—Fifth Edition. E. Noble Chamberlain, M.D., M.Sc., F.R.C.P., Senior Lecturer in Medicine, University of Liverpool. The Williams and Wilkins Company, Baltimore, 1952. 479 pages, 354 illustrations, 19 in color, $8.00.

This is an English attempt to compress the whole of physical diagnosis into one compact volume for the benefit of medical students taking the first course in clinical medicine.

The book is well printed on good grade glossy paper and is well supplied with adequate illustrations (354 illustrations in 451 pages). Other features include a table of symptoms with suggestions for leading questions and area of examination and a glossary of medical terms with their etymology.

Although the try is a worthy one, the reviewer feels that the book cannot be recommended to replace existing American texts on physical diagnosis. The material is stretched too thin and the resultant lack of completeness and detail serves to emphasize the regional differences in teaching.

THE GOLD-HEADED CANE. William Macmichael, M.D. A new edition with a foreword by James J. Waring, M.D., and a preface by William J. Kerr, M.D.; containing the text and illustrations of the fifth edition, including the introduction by George C. Peachey and his annotations. Charles C. Thomas, publisher, Springfield, Illinois, 1953. 186 pages, $6.50.

The original Gold Headed Cane belonged to John Radcliffe, an eminent English physician for whom Radcliffe Library and Radcliffe Infirmary at Oxford are named. On his death in 1714 it passed to Richard Mead (d. 1754) and then in succession to Anthony Askew (d. 1774), William Pitcairn (d. 1797), his nephew David Pitcairn (d. 1809), and finally to Matthew Baillie (1761-1823). After Dr. Baillie's death the Cane was presented by his widow to the New College of Physicians and has reposed for many years in the Museum of the Royal College of Physicians in London. It became widely known following the publication in 1827 of *The Gold-Headed Cane* by an anonymous author, soon identified as Dr. William Macmichael. The work was so popular that a second edition was issued in 1828, and later ones in 1884, 1915, 1923, 1932 and—the present seventh edition—in 1953. It consists of biographies, told in the first person by the Cane, of the five owners, and contains a great deal of material of historical interest concerning the men themselves, their contemporaries and times. The five physicians were all highly successful practitioners of medicine, most of whose work centered about St. Bartholomew's Hospital in London, and reflected the best medical standards of their times, although none contributed much to medical literature or to scientific advancement. As a group they stand for excellence in the art of medicine, of which the Cane has become a symbol.

In 1939, Dr. William J. Kerr, Professor of Medicine at the University of California Medical School established the ceremony, held annually since then, in which a newly designed Gold Headed Cane is awarded to a member of the graduating class selected by his classmates and by the faculty on the basis of "the student's interest in the welfare of his patients during his entire clinical experience."

The emphasis then is not upon pure scholarship but rather, as Dr. Kerr says in the preface, on the student's promise to become a successful physician, which rests more often "upon his ability to apply knowledge and to express those qualities of heart and hand which endear him to his patients." Honorable mention is given to two other students. At the annual ceremony, a speaker of distinction (the first was the late Herbert C. Moffitt) gives an address and is himself presented with a replica of the Cane.

The present volume is attractively printed and bound. It contains a foreword by James J. Waring, a preface by Dr. Kerr, and an introduction by George C. Peachey, giving additional biographical material on the five owners of the Old Cane. For medical educators and other physicians interested in the historical aspects of medicine, this work should be a valuable acquisition.

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THE SCALP IN HEALTH AND DISEASE. Howard T. Behrman, A.B., M.D., Assisant Clinical Professor of Dermatology, New York University Post-Graduate Medical School. With 312 illustrations. The C. V. Mosby Company, St. Louis, 1952. 566 pages, $12.75.

In this handsomely bound and well-printed book, Dr. Behrman presents a distinctive addition to the dermatologic literature. The 540 pages of text are interspersed with 312 photographs and drawings, many of which are quite unusual and all of which are pertinent and instructive. Since the text was written by a single author, it enjoys the advantage of a consistent literary style. Dr. Behrman's writing is quite lucid and oftentimes somewhat restrained in that the findings and opinions of others are fairly presented without strong condemnation or recommendation. The entire contents of the book are concerned with the hair and scalp and are divided into nine chapters and an appendix. The first chapter has in addition to Embryology, Anatomy, and Physiology of the hair and scalp, an interesting section concerning the anthropological considerations of hair form and distribution. Chapter two discusses the normal care of the scalp along with the action of some of the constituents of hair dressing preparations. Chapter three, labeled Alopecia, is perhaps one of the most useful in the book, for in one chapter many different aspects and opinions concerning the various forms of Alopecia are considered at length. The fourth chapter is a short one about Seborrhea and the Seborrheic diatheses. The fifth chapter labeled Infections covers the known infections usually found in the scalp, and many of those that only occasionally or indirectly are manifested in the scalp. Chapter six is cautiously labeled Scalp Disorders of Psychogenic Origin (Proved or Presumptive).

The last chapter on Neoplasms is as inclusive in its subject matter as the other chapters. Preceding an adequate index is the interesting and useful appendix containing 243 formulae of various hair and scalp preparations arranged as to the type of preparation, i.e.: shampoos, lotions, etc. In many instances the name of the originator is given with his particular formula, adding to the interest and historical value of the section. At a glance of the appropriate section one can see the similarity of the various modifications that have been used and select the particular variation most suited to the needs at hand. However, the formulary does not contain some of the more recent preparations that have been described. This book is a valuable addition to any dermatologic library and adding to its usefulness is the large classified bibliography that is found at the end of each chapter.

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THE PRINCIPLES AND METHODS OF PHYSICAL DIAGNOSIS—Correlation of Physical Signs with Physiologic and Pathologic Changes in Disease. Simon S. Leopold, M.D., Associate Professor of Clinical Medicine, School of Medicine and Graduate School of Medicine, University of Pennsylvania. With a **Chapter on Sounds for the Thorax: Acoustic Principles** by S. Reid Warren, Jr., Sc.D. in E.E., Professor of Electrical Engineering, Moore School of Electrical Engineering, University of Pennsylvania. 390 illustrations, 10 Color Plates. W. B. Saunders Company, Philadelphia, 1952. 430 pages, $7.50.

It is the firm belief of the author "that the principles and methods of physical diagnosis should be taught by correlating physical signs with physiologic and pathologic changes in disease." With this in mind, he has compiled a very workable textbook for the second year student.

He has made maximum use of illustrations, gathering together a comprehensive group of photographs, some in full color, drawings and roentgenograms. In many cases, these serve as part of the text, and the reading matter, while entirely adequate, is pared down to the essentials. The book is well—and simply—organized and the table of contents provides a ready reference. The chapter on The History has been placed at the end of the book with the idea that history-taking, as such, should not begin until the student can correlate some knowledge of disease seen at the bedside with the preclinical sciences.

There is an interesting chapter on acoustic principles related to sounds from the thorax, and the line drawings illustrating muscle testing are especially informative.

This book can be well recommended to second year medical students and to teachers of medicine. It may also be used as a reference by the physician in practice.

TRANSACTIONS OF THE AMERICAN COLLEGE OF CARDIOLOGY—Volume II—1952. Bruno Kisch, M.D., Editor. American College of Cardiology, 140 West 57th Street, New York, N. Y., 1953. 252 pages, $5.00.

This volume includes proceedings of the last two meetings of the College of Cardiology. Papers read at the meetings are arranged in order of presentation but in varying detail; some are published in toto, while others appear in form of very brief summaries. Most of the papers contain either data published in more detail elsewhere, or represent reviews of various subjects. Consequently, one finds relatively little original and stimulating material, and it is doubted whether this volume will be of interest to many outside the membership of the College of Cardiology.

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AN ATLAS OF SURGICAL EXPOSURES OF THE EXTREMITIES. Sam W. Banks, M.D., Associate Professor of Orthopedic Surgery, Northwestern University Medical School; and Harold Laufman, M.D., Ph.D., Associate Professor of Surgery and Director of Experimental Surgery, Northwestern University Medical School. W. B. Saunders Company, Philadelphia, 1953. 391 pages with 552 illustrations on 179 plates, $15.00.

This atlas of surgical exposures of the extremities fulfills a pressing need that has been recognized for some years. There have been several similar works published in the last few years but this particular one appears superior to any of the others. The anatomical illustrations are perfect representations not only of the anatomy but also of the practical surgical application of anatomical knowledge to the specific exposure desired for any given surgical procedure. The text is clear, concise and correlated perfectly with the anatomical illustrations.

The book is of such value that the reviewer recommends it highly to anyone interested in the surgery of the extremities and particularly to any student or practicing orthopedic surgeon. No fault can be found with the descriptive text or with the anatomical illustrations.

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FROM THE WORKSHOP OF DISCOVERIES. Otto Loewi, Research Professor of Pharmacology, New York University College of Medicine. University of Kansas Press, Lawrence, 1953. 62 pages, $2.00.

This small volume by a famous pharmacologist is made up of three lectures to medical students. The author elaborates broadly on his philosophy, discussing his vewpoints on medicine and man, on medical research and medical students themselves.

The book will prove of greater interest to the medical philosopher than to the medical technician, even though the third lecture deals with problems in the field of adrenal function.

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SECTIONAL RADIOGRAPHY OF THE CHEST. Irving J. Kane, M.D., Consultant in Chest Diseases, U. S. Naval Hospital, St. Albans, N. Y. Springer Publishing Company, Inc., 44 East 23rd Street, New York, 1953. 154 pages, $7.50.

This is a handsomely prepared monograph dealing with tomography or planigraphy. Following a section on basic principles, there is a collection of roentgenograms, well produced, showing the values of sectional radiography as used by the author.

The illustrations are in "negative" form (i.e., like the original films) and most are clear. The legends are excellent. It is suggested that in future editions, the author might stress the benefits of simpler methods of examination such as posterior lordotic projections, heavy density stereoscopic projections, heavy density and oblique and lateral projections. The time and expense involved in body section radiography, and the radiation dosage often received by the patient are perhaps not adequately emphasized. There are approximately one hundred illustrations, and these alone should make the book of considerable interest to students and beginners in radiography.

The author is a chest physician in New York City. There is an adequate bibliography and index.

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EXCERPTA MEDICA—CANCER (EXPERIMENTAL AND CLINICAL)—Section XVI, Vol. 1, No. 1, July, 1953. Published by Excerpta Medica, N. V., 111 Kalverstraat, Amsterdam C. (The Netherlands). Published monthly. Vol. 1, July to December, 1953, $5.00, succeeding volumes, $10.00 per year. Aided by grants from the National Cancer Institute of the Public Health Service and the American Cancer Society.

The value of an abstract journal in a limited field in medicine is well recognized. The wisdom of attempting an abstract journal in a field as broad as cancer is a subject of some debate. The monograph under review consists of some 95 pages and 424 abstracts. There are about 60 lines to the page. The printing is clear and the paper excellent.

All of the abstracts are in English. They are made by physicians in various parts of the world, ranging from a Dr. Op de Coul in Almelo to a Dr. Schut in Anoka.

It is unavoidable that some of the abstracts are rather uncritical and perhaps poorly selected. On the whole they appear to be adequate and reasonably complete. Probably a useful work for libraries.

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PRACTICAL X-RAY TREATMENT—Fourth Edition. Arthur W. Erskine, M.D. The Bruce Publishing Company, St. Paul, 1953. 195 pages, $5.00.

This is the fourth edition of a well known and useful manual on x-ray treatment. After a section on mechanical factors, the author deals with considerations of skin dose and depth dose. There is a good discussion of scattered radiation. The effects of x-rays on tissue are briefly outlined. Suggestions regarding the treatment of skin diseases, infections, various benign lesions and malignant lesions are then given. Many of the techniques used have stood the test of time. However, not many radiation therapists will be as enthusiastic for transvaginal roentgen therapy as is the author.

There are references at the end of each chapter and there is a good index. The work can be recommended to students, especially those in radiology.

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INFLUENZA AND OTHER VIRUS INFECTIONS OF THE RESPIRATORY TRACT. C. H. Stuart-Harris, M.D., F.R.C.P., Professor of Medicine, University of Sheffield. Distributed by Williams and Wilkins Company, Baltimore. Edward Arnold & Co., London, 1953. 235 pages, $6.00.

Stuart-Harris is a real authority on the subject, as he has done original investigation of a high order, on influenza and other virus infections. Although the book deals with all phases of the subject, including the clinical side, a special feature is a discussion of the development of knowledge and understanding of the viruses which are responsible for these diseases. The recovery of the influenza virus in the ferret in the thirties and the subsequent advancement of knowledge makes a really exciting story. The book is thoroughly up to date and gives the latest information on modern methods of virus diagnosis. In addition to influenza, colds, psittacosis, Q fever and allied conditions are thoroughly dealt with in interesting fashion. There are numerous excellent illustrations, lists of references at the end of each chapter, and an index.